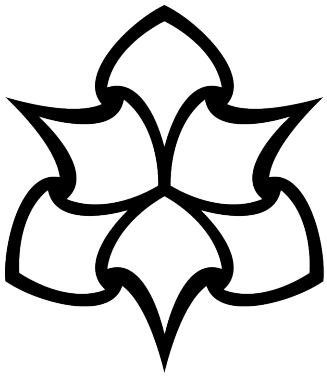

The control of type 2 diabetes with specific references to *Nigella sativa* seed and Ajwa dates

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Abstract

Diabetes occurs when the pancreas does not secrete sufficient insulin or when cells become resistant to insulin regardless of the quantity of produced. Diabetes in Saudi Arabia is reported to have reached epidemic proportions. This ever-increasing incidence has been blamed on low levels of physical activity and high levels of obesity.

The effects of *Nigella seeds* and Ajwa dates on blood glucose levels in patients with type 2 diabetes and the possible beneficial effects on the complications associated with type 2 diabetes were investigated.

This study used a randomised clinical intervention trial. 75 Saudi adults, with type 2 diabetes, aged between 18 and 60, were divided into 3 groups. Groups were assigned the following diets; Group D-NS - the modified diet supplemented with 2g of *Nigella sativa* seeds daily; Group D-AJ - the modified diet supplemented with 1 Ajwa date daily; Group D-D the modified diet without supplements. The study period was 12 weeks. Anthropometric measurements and blood samples for the determination of HbA1c, fasting blood sugar were taken at the beginning and end of the study. A similar group of 75 healthy volunteers was recruited in the UK for comparative studies.

There was a significant decrease in the levels of FBG ($P < .001$), 2PPBG ($P < .001$), and an improvement in some markers of glycaemia plus better control of BGL and HbA1c in Group D-NS compared to the levels in Groups D-AJ and D-D. Thus following a modified diet supplemented with *Nigella* seeds may have a role in controlling the outcomes for type 2 diabetes patients. Large scale clinical trials to determine the optimum dose and duration of *Nigella* seed diet treatments are now needed.

The modified diet supplemented with Ajwa dates apparently had no advantages. Further investigations in relation to the quantity and frequency of use of Ajwa dates as a dietary supplement are essential before any conclusions can be drawn as to their effectiveness.

Declaration

I declare that this thesis is all my own work and has not been copied from any other sources, or accepted for any other degree in any University. To the best of my knowledge this thesis contains no material written or distributed previously by any other parties, apart from where I have otherwise stated.

Reham Algheshairy

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List of Abbreviation

AP	**Arterial pressure**
BHF	British Heart Foundation
BGL	Blood Glucose Level
BMI	Body mass index
BNF	British Nutrition Foundation
BP	Blood pressure
CHOs	Carbohydrates
CI	Confidence intervals
CVD	Cardiovascular disease
DASH	Dietary Approaches to Stop Hypertension
DBP	Diastolic blood pressure
DM	Diabetes Mellitus (DM)
DRVs	Dietary Reference Values
FBG	Fasting blood Glucose
FDA	Food and Drug Administration
GI	Glycaemic Index
HbA1c	Glycated haemoglobin
HDL	High density lipoprotein
IDF	Insoluble Dietary Fibre
IDF	The International Diabetes Federation
IDDM	Insulin Dependent Diabetes Mellitus
KSA	The Kingdom of Saudi Arabia
LDL	Low density lipoprotein
M	Mean
mg/dl	Milligram/decilitre
mmol/L	Millimole

NICE	The National Institute for Clinical Excellence
NIDDM	Non-insulin Dependent Diabetes Mellitus
NO	Nitric oxide
NsO	*Nigella sativa* oil
Ns	*Nigella sativa* seeds
PA	Physical activity
PDE	Phoenix Dactylifera Extract
RCT	Randomized control trial
SA	Saudi Arabia
SBP	Systolic blood pressure
SDF	Soluble Dietary Fibre
SMBG	Self-monitoring blood glucose level
SMOH	The Saudi Ministry of Health
SD	Standard deviation
SPSS	Statistical Package for the Social Science
TG	Triglycerides
TC	Total cholesterol
T2DM	Type 2 Diabetes Mellitus
TAC	Total antioxidant capacity
WHO	The World Health Organization
2hPP	Two hour postprandial

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1.1. Introduction

Cases of type 2 diabetes are on the rise across the world, especially in Saudi Arabia, due to the lack of awareness of the disease, the increasing prevalence of obesity, unhealthy dietary intake and poor lifestyle habits, such as lack of physical exercise.

Traditional herbs, from natural sources, are often used as an alternative to medication to treat different diseases for a variety of reasons. Some of these include the fact that they are safe from side effects, easy to get hold of and cost less than most medications. Raw *Nigella sativa* (Ns) seeds were used as one of the dietary supplements in this study in order to make it easy for the participants to use them. According to Islamic history and tradition, it is widely believed that *Nigella sativa* has a wide range of health benefits, which could be used to help diabetic patients (see chapter 2, section 2.9). This was one of the reasons that Ns was used as a dietary supplement as part of this study. Although there are many studies (refer to page 39 in Chapter 2) that suggest that *Nigella sativa* has a beneficial effect on BGL, this study differs from others because the researcher examined the effect of raw *Nigella sativa* seeds on BGL, rather than the effect of a Ns derived substance (such as powder, oil, extract or a tea bag). This was done for several reasons. Firstly, to allow all the potential benefits that come from chewing the whole seed, as a fresh herb to be observed. Secondly, to allow all the bioactive natural components present in Ns and the vitamins, fibres, natural antioxidants, fats and minerals to work together, to see whether they had a beneficial effect on diabetic patients, and thirdly, because Ns can be easily bought and found.

The reason for using Ajwa dates and *Nigella sativa* seeds as dietary supplements in this research is due to the fact that both are natural products, containing polyphenol and antioxidant components, which could possibly be used as a safer alternative to chemical medications (as explained in chapter 2). Moreover, both Ajwa and *Nigella sativa* have been the subject of experiments on animals in relation to their potential anti-diabetic effects (Fararh *et al.*, 2004 and Ragab *et al.*, 2013). However, although *Nigella sativa* has since been used in human studies and clinical trials (from 1997 to 2015, see chapter 2, section 2.9), there remains a gap in research on Ajwa dates

and their effects on humans. It is for this reason that one of the research questions that this thesis aims to address is 'Does Ajwa have a potential effect on blood glucose levels?'

This thesis focuses on the effect of dietary factors (raw *Nigella sativa* seeds and Ajwa dates) on the blood glucose profile of patients with type 2 diabetes and on healthy participants. The non-diabetic healthy participants were examined in order to measure their blood glucose profile and compare the effects of different dietary factors on their BGL. This study consists of two trials: trial 1 was an examination of the effects of a modified diet or modified diet supplemented with either Ajwa dates (1 per day) or *Nigella sativa* seeds (2g/day) for 12 weeks on diagnostic markers of type 2 diabetes in diabetic patients: trial 2 was an examination of the effects of a modified diet or modified diet supplemented with either Ajwa dates (1 per day) or *Nigella sativa* seeds (2g/day) for 12 weeks on diagnostic markers of type 2 diabetes in healthy participants.

The findings in this thesis contribute to human nutrition studies on the possible beneficial effects of *Nigella sativa* seeds and Ajwa dates when used as supplements to a diet modified for consumption by patients with type 2 diabetes patients. The results clearly show that a modified diet designed specifically for KSA citizens with diabetes and taking into account local preferences and ethnic requirements is beneficial. The study also supports reports that *Nigella sativa* seeds added as a supplement to the modified diet is even more beneficial for diabetes patients.

1.2. Hypothesis:

This study proposes that modification of a basic diabetic diet by the addition of certain foods; *Nigella sativa* seeds or Ajwa dates, will significantly improve the control of sugar levels in type II diabetic patients and healthy individuals.

1.3. The general Aim of the study

The project has two aims;

first; to investigate the regulatory effects of the consumption of *Nigella sativa* seeds and Ajwa dates on blood glucose levels in diabetic patients with type 2 diabetes; second; to investigate whether these dietary supplements have beneficial effects in controlling the complications that are associated with type 2 diabetes.

Aims

- To develop a modified diet regime which is specifically applicable to the residents of the KSA taking into account local preferences, food taboos and eating habits.
- To test the modified diet in the KSA in diabetic patients with type 2 diabetes by monitoring fasting blood glucose and postprandial blood glucose levels and comparing these to a control group receiving the basic diet.
- To determine whether adding Ajwa dates or *Nigella sativa* seeds to the modified diet improves the effects of the modified diet.
- To investigate the relationship between the dietary factors (*Nigella sativa*, Ajwa dates) and postprandial blood glucose amongst intervention group if a relationship is demonstrated.

Objectives

The main objectives of this study were

- To study the effect of three diet regimes: a modified diet, a modified diet supplemented with 2g/daily *Nigella sativa* seeds*,* a modified diet supplemented with 1 Ajwa date/daily on the glucose profiles of Type 2 diabetes mellitus patients. To study the effect of three diet regimes: a modified diet, a modified diet supplemented with 2g/daily *Nigella sativa* seeds*,* a modified diet supplemented with 1 Ajwa date/daily on the

glucose profiles of healthy participants (non diabetic).

- To study the effects of a modified diet, a modified diet supplemented with *Nigella sativa* seeds*,* a modified diet supplemented with Ajwa dates and on blood pressure (SBP and DBP) of type 2 diabetes mellitus patients.
- To recommend the appropriate dietary intake of *Nigella sativa* seeds*,* Ajwa dates and modified diet for the amelioration of the symptoms associated with type 2 diabetes mellitus.

1.4. Contribution to Knowledge

There is great interest in the contribution of dietary factors to the treatment of type 2 diabetes. Some studies have shown that a plant-based diet has proactive effects against the development of metabolic complications such as insulin resistance in type 2 diabetes. Indeed these beneficial effects have been related to the presence of polyphenolic compounds, which possess a wide range of biological properties including antioxidant and insulin-sensitizing activities. (Jung *et al*., 2006)

This research will provide a significant contribution to the understanding of the effects of dietary factors in the control of postprandial blood glucose levels in type 2 diabetes, specifically, *Nigella* seeds and Ajwa dates. Furthermore, it will broaden our knowledge of how these dietary factors may regulate blood glucose and lipid levels. Adding *Nigella* seeds to the diet has been shown to control hyperglycaemia in patients with type 2 diabetes, however there are no similar reports in relation to Ajwa dates, hence this study will add this knowledge. Additionally, the study may demonstrate that the natural fibre, antioxidant effects and polyphenolic compounds in Ajwa dates contribute to the control of factors which influence the diabetic complications and improve glucose metabolism and insulin sensitivity in diabetic patients. Accordingly, dietary modification programmes, if beneficial, may be employed as an alternative approach to control the risk of type 2 diabetes in clinical practice.

1.5. Overview of thesis chapter

The study consists of 6 chapters:

Chapter 1 Introduction, an overview of the introduction to type 2 diabetes, aims, objectives and hypothesis of this study and its contribution to knowledge.

Chapter 2 Literature Review, which shows the background of type 2 Diabetes and the classification of the different types of diabetes and the possible symptoms. It also presents the definition of T2DM and the prevalence of diabetes, with the discussion focussing specifically on the context of Saudi Arabia. This chapter also highlights the possible risk factors related to T2DM and the lifestyle modifications. The second section of chapter 2 presents details of *Nigella sativa* Seeds (Ns), their nutritional value and the possible benefits of *Ns* consumption on Blood Glucose levels (BGL) and Blood Pressure (BP). The third section describes Ajwa Dates (AJ), their chemical composition, nutritional properties and reported health benefits.

Chapter 3 Methodology, illustrates the process of obtaining ethical approval for the study from Manchester Metropolitan University (MMU) and from AL-Noor hospital of Makkah in Saudi Arabia, the study design and population for Trial 1 (Diabetic Group) and Trial 2 (Healthy Group). It also presents the inclusion and exclusion criteria for Trials 1 and 2, explains the recruitment and selection criteria for the diabetic and healthy participants and provides information about determination of sample size and study duration. This chapter also covers data collection and processing, how the questionnaire was designed and how the diet for the trials was developed. Measurements for Trial 1 were: blood pressure, blood glucose profile (FBG and 2hPP blood glucose) and HbA1c levels. The measurements for Trial 2 were: blood glucose profile (FBG and 2hPP blood glucose). This chapter then presents the validity and reliability of the study, participants' compliance with appointments, treatments, measurements and diet and finally the statistical analysis methods.

Chapter 4 Findings; provides a detailed comparison of the results from the Diabetic groups (trial 1) analysing the characteristics of Diabetic Patients,

their Blood Glucose Profile (FBG, 2hPP), Haemoglobin (HbA1c) levels and Blood Pressure (Systolic and Diastolic Blood Pressure). The second part of this chapter looks at the findings for trial 2, Blood Glucose Profile (FBG and 2hPP). Chapter 4 concludes with a comparison of the results for diabetic patients and healthy participants (Blood Glucose Profile) FBG, 2hPP blood glucose levels.

Chapter 5 Discussion; discusses the demographic and lifestyle data, which includes age, duration of diabetes, smoking status, education level, physical activity, Body Mass Index (BMI) and measuring blood glucose level using Self monitoring Blood Glucose (SMBG). The chapter then goes on to discuss the individual parameters in the diabetic group (Trial 1) FBG, 2hPP, HbA1c and blood pressure measurements SBP and DBP. Then the discussion moves onto the demographic and lifestyle data of the Trial 2 group and discusses the individual parameters in the Healthy groups (FBG, 2hPP) and sums up with a general discussion.

Chapter 6 Conclusion; presents the limitation of the thesis, discusses the suggestions for future studies and presents the overall conclusion before listing several public health recommendations.

Chapter 2 Literature Review

2.1. Introduction

This chapter will first provide some background information on Diabetes Mellitus (DM) and then explains the difference between Type 1 and Type 2. It will then move on to discuss the prevalence of T2DM in the Kingdom of Saudi Arabia and identify some of the associated risk factors, which include obesity, diet, level of physical activity and level of education. The chapter will then discuss the lifestyle modifications that are needed to control and manage Type 2 DM before presenting the current literature on the effects of *Nigella sativa* seeds and Ajwa dates on Type 2 DM.

2.2. Background of Diabetes Mellitus

Diabetes Mellitus (DM) can be defined as a metabolic disease that occurs due to a variety of factors including chronic hyperglycaemia and defects in both or either insulin secretion and insulin action (Haslett *et al*., 2002). A sufferer of DM can live normally, although the condition is permanent. The World Health Organization (WHO) have stated that HbA1c levels can be used as a diagnostic test for diabetes, whereby the cut-off point for diagnosing diabetes is 48 mmol per mol (6.5%)(WHO, 2011). They recommend that diabetic patients should measure their glycated haemoglobin (HbA1c) levels every 3 months in order to help sufferers of diabetes control their plasma glucose level. The standard level of Fasting Blood Glucose (FBG) for diabetes should be FBG ≥7.0 mmol/l and for the two hours postprandial should be ≥11.1 (Matthews *et al.,* 2008).

The pancreas (beta cells) secretes a peptide hormone known as insulin and the primary function of this hormone is to remove glucose from the bloodstream and to transfer it to the cells of the body for metabolism. There are 2 forms of diabetes, type 1 and 2.

In patients with type 2 diabetes, the glucose absorbed from the intestine enters the bloodstream and this should stimulate insulin secretion by the pancreas, which then stimulates uptake of the glucose by cells and conversion to body fat (Matthews *et al.,* 2008). In the type 1 and type 2 diabetic patient, the pancreas cannot produce insulin in sufficient quantities (or produces none at all) so the absorbed glucose remains in the blood stream. This results in higher

blood glucose levels, which is the diagnostic measure that is used to identify diabetes patients. In type 1 diabetes patients, there is no insulin or such low levels that it is not effective usually as result of an inherited defect but occasionally as a result of disease (Matthews *et al*., 2008). These patients are treated with insulin. In type 2 diabetes, the insulin insufficiency occurs as a result of damage to the pancreas, which is not inherited. Type 2 usually occurs in later life because the loss of insulin production is gradual (Geissler and Powers, 2005; Matthews *et al*., 2008).

Mann and Truswell (2007); Geissler and Powers (2005) explain the differences between Type 1 [Insulin Dependent Diabetes Mellitus (IDDM)] and Type 2 [Non-insulin Dependent Diabetes Mellitus (NIDDM)]. Type 1 (IDDM) occurs in about 10% of all cases and is most common in childhood and adults over 40 in the white population and adults over 25 in the South Asian population. On the other hand, Type 2 (NIDDM) is the most prevalent type of diabetes, which occurs in about 90% of all cases and is most common in adults. The symptoms for both types of diabetes include thirst, urination, slow healing, blurred vision, thrush or genital itching, tiredness and weight loss (Matthews *et al.,* 2008). However, one of the main differences between the two types of diabetes is that in Type 1 (IDDM) the above symptoms come quickly while in Type 2 (NIDDM), the symptoms develop slowly. It is for this reason that Wass and Shalet (2002) claim that sufferers of T2DM face a heightened chance of complications as the condition may remain undiagnosed for a long time. Moreover, the treatments for Type 1 (IDDM) include an insulin injection with a dietary plan considering individual nutritional needs, while treatments for Type 2 (NIDDM) not only sometimes include an insulin injection, but also a diet plan, doing physical activity and reducing weight. Furthermore, Kumar and Clark (2005) have identified advanced age, obesity, family history and ethnicity (Common in South Asian, African-Caribbean and white populations) as the four key factors in the onset of type 2 diabetes.

2.3. Prevalence of Type 2 Diabetes

According to the WHO (2016), approximately 1.5 million people died globally due to high blood glucose levels in 2012 and the incidence of diabetes in the same year was 3.7 million. Worldwide, countries now spend from one quarter to one sixth of their annual health care funds on treating the various forms of diabetes. The WHO (2016) recently reported that the prevalence of diabetes in adults worldwide rose to 422 million in 2014. Furthermore, in 2014, 13.7% of the incidents of diabetes were found in the Eastern Mediterranean Region (places such as Kuwait, Bahrain, Oman, Saudi Arabia, Egypt, Qatar, Jordan and Iraq).

In developing nations, individuals in their prime, aged from thirty-five to sixty-four, are most commonly struck down with diabetes. It has been affirmed by the World Health Organisation (2016) that developing nations will see a rise in the incidence of diabetes, especially low income countries. Nine out of every ten cases of the two forms of diabetes are the common Type 2 form of the condition, which brings with it an elevated risk of cardiovascular conditions and early morbidity (WHO, 2016). The WHO (2017) predicted an increase in cases of diabetes by 2025, which would make diabetes the 7th leading cause of death in the world (WHO, 2017).

Since 2000, the International Diabetes Federation has produced a series of IDF Diabetes Atlases, with the latest seventh edition released in 2016, which shows the development of diabetes across the world (IDF 2000; IDF 2016). These reports show that the incidence of diabetes has been increasing worldwide throughout the period covered by the reports, but more interestingly the predicted incidences for the year 2050 has increased significantly. The atlases also show the reported incidence of diabetes for individual countries. According the International Diabetes Federation (IDF) the prevalence of diabetes in Saudi Arabia is very high and predicted to increase even further over the year.

2.4. Type 2 Diabetes in Saudi Arabia

The Kingdom of Saudi Arabia (KSA) is one of the biggest and richest countries in the Middle East as it is one of the leading oil-producing countries. Over the past five decades, it has made considerable progress as a result of its intense industrialisation and lifestyle modifications (Bahijri *et al.*, 2016), which Al-Daghri *et al*, (2011) claim has resulted in a heightened incidence of Type 2 DM. This rationale is supported by the findings of Al Nozha *et al,* (2004) (see table 2.1) and various other studies (see table 2.2), which suggest that the prevalence of T2DM is higher in urban areas when compared with rural areas of SA.

Table 2.1. The prevalence of type 2 Diabetes in Saudi population (Al-Nozha et al, 2004)

Saudi regions	Prevalence of type 2 Diabetes
Urban population	25.5%
Rural areas	19.5%
Northern	27.9%
Eastern	26.4%
Southern Region	18.2%

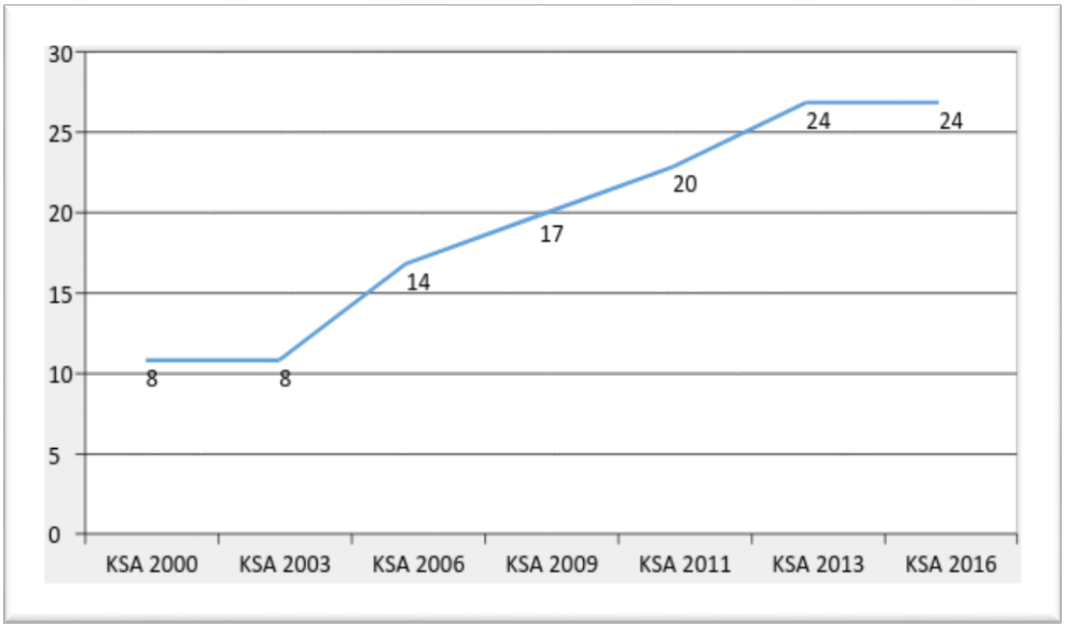


Figure 2.1. Incidence of type 2 Diabetes in the KSA 2000 – 2016 (data taken from the IDF Atlases for each year indicated)

Figure 2.1 shows the incidence of type 2 diabetes reported for the KSA between 2000 and 2016. This data demonstrates that the incidence of type 2 diabetes in the Kingdom of Saudi Arabia was low, 8-11% in both 2000 and 2003 but then a rapid rise occurred between 2003 and 2013 when the cases of diabetes reached 24%. From figure 2.1 it appears that the incidence of diabetes between 2013 and 2016 remained constant in Saudi Arabia. Interestingly this rise in the incidence of diabetes appears to be directly related to the increase in GDP (Gross Domestic Product) which also began to rise sharply after 2000 and peaked in 2012 (Fig 2.2)

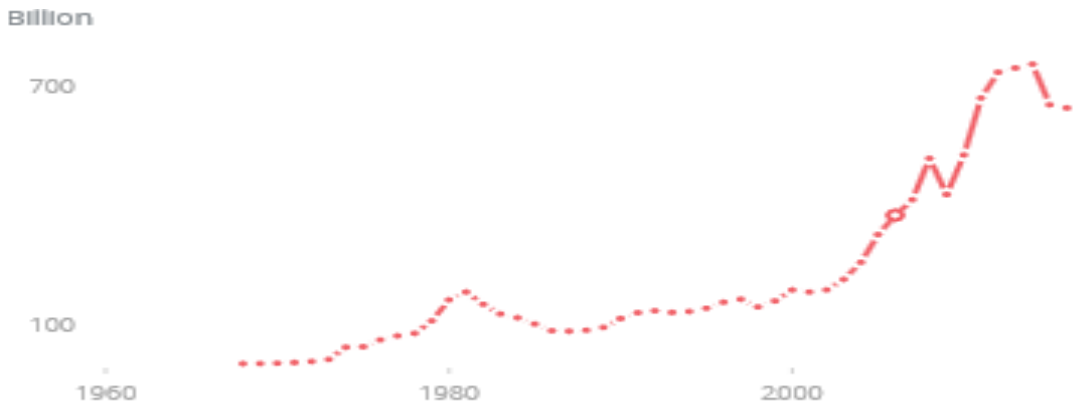


Figure 2.2. GDP (Gross Domestic Product) for the Kingdom of Saudi Arabia (World Bank)

These data support the general contention that the rise in Type 2 diabetes in the Kingdom of Saudi Arabia is associated with an increasingly sedentary lifestyle, which is related to the increase in personal income. The data presented in this thesis is consistent with the hypothesis that type 2 diabetes is related to lifestyle; hence education programmes which could potentially result in changes in lifestyle should generate improvements.

A rise in diabetes among the adult population has been observed in research conducted since the late 1980s (Wilson, 2010). In 2011, an epidemiological research study on diabetes carried out by Al-Daghri *et al*, (2011) aimed to examine the position of the Saudi Arabian people and whether the initiatives undertaken by the healthcare community and the Ministry of Health had had any beneficial effects. They concluded that Type 2 DM was found in approximately 20% of the country's adult population (Al-Daghri *et al.*, 2011).

In 2011 the International Diabetes Federation (IDF) placed the KSA within the top 10 countries in the world with the highest prevalence of diabetes (Whiting *et al.*, 2011). In 2015, the figure had not changed much (see figure 2.3 below) as it stood at 23.9% according to a report by Naeem (2015).

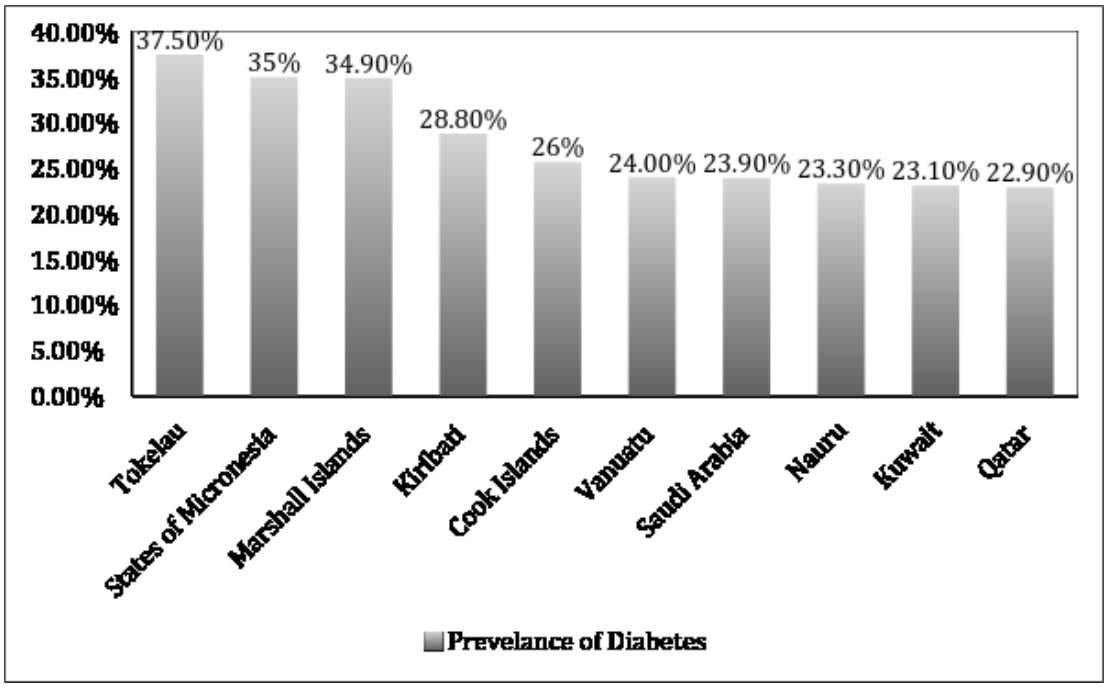


Figure 2.3.The population prevalence of Diabetes (Naeem, 2015)

Furthermore, Albakr *et al*., (2013) observed a rise in the awareness of diabetes, possibly indicative of Saudi Arabia's improving health care system. However, Al-Quwaidhi *et al* (2014) reported that the prevalence of some risk factors for T2DM in the KSA such as obesity had been estimated to be among the highest in the world. In addition, the prevalence of obesity among females is higher than males in Saudi , that would increase the risk of having T2DM in female population (AL-Quwaidhi *et al* ., 2014). Bahijri *et al,* (2016) claims that one of the reasons for this could be the lack of development programmes designed to prevent or reduce the prevalence of T2DM in Saudi Arabia (SA). The above mentioned studies (Al-Quwaidhi *et al.*, 2014 and Bahijri *et al.,* 2016) claim that the prevalence of diabetes in SA has reached epidemic proportions. Almalki *et al,* (2011) further adds that this is due to Saudi's not using the medical preventative services, despite the fact that they are covered by a free national health system.

In 2016, the World Health Organisation reported that the prevalence of diabetes in SA stood at 14.4% with the percentage of males with diabetes being higher than females (14.7% and 13.8% respectively). They (ibid, 2016) claim this could be due to an increase in obesity level (33.7%) amongst the Saudi adult population (WHO, 2016).

Table 2.2.Studies of type 2 diabetes in Saudi Arabia

Study	Country	Samples Size			Age	Diagnostic Criteria	Prevalence of diabetes		
		Male	Female	Total			Male	Female	Total
Bahijri et al 2016	SA (Jeddah)	667	752	1419	≥18	ADA FBG HbA1c	12.9%	11.4%	24.3 %
Al Zahidy et al 2017	SA	1150	1670	2820	20 – 70	_	40.8%	59.2%	
Al-Rubeaan, et al. 2015	SA	28238	22226	50464	≥25	_	46%	44%	
Bani 2015	SA (Jazan)	146	102	248	≥18	WHO	9%	19%	
Algurashi et al 2011	SA	768	1024	1792	≥20	Self reporting	34.1%	27.6%	
Al-Nozha 2004	SA	2099	1889	4004	30-70		26.2%	21.5%	23.7 %
Karim 2000	SA	1683	2064	3747	0 to 70	_	8.52%	19.48 %	28%
El-Hazmi et al 1998	SA	-	-	25337	0 to 77		5.86%	4.83%	
Al-Nuaim et al 1997	SA	-	-	13177	>15		12%	14%	

2.5. Treatment of type 2 Diabetes

Type 2 diabetic patients can be treated in the early stages of the disease, especially if it is diagnosed early. There are different treatments available, which work to manage blood glucose levels and to reduce the development of the disease itself. Among the actions that diabetics are encouraged to take is measuring their blood glucose levels as a daily routine, as this could help the patients to check the ideal level for fasting blood glucose (FBG 4 to 7 mmol/L) and 2 hour postprandial (2hPP < 8.5 mmol/L) blood glucose levels. Furthermore, in order to obtain a reliable measurement for BGL, diabetics are encouraged to measure the glycated blood levels (HbA1c) at least every 3 months. They should check to ensure that HbA1c levels should be between 6.5% (48 mmol/mol) to 7.5% (58 mmol/mol)(WHO,2011).

Lifestyle and dietary modification are also among the most common treatments for type 2 diabetic patients. Diabetics are encouraged to maintain a healthy varied diet, physical exercise and a healthy weight (BMI 18.5-25 kg/m2). The National Institute for Clinical Excellence (NICE, 2009) recommended that providing healthcare advice is an excellent means by which diabetic patients can be provided with the means to manage their disease by being made aware of such lifestyle and dietary modifications. Education allows them to understand how to treat themselves in a variety of ways. They can be taught to understand nutritional information, how to follow a dietary plan, how to administer their medication and how to monitor their BGL at home using self-monitoring blood glucose equipment (SMBG).

In addition, for those diabetic patients with uncontrolled type 2 DM, who cannot control their BGL with a controlled diet alone, the main treatment for them is insulin medication (drugs to help the patients manage the BGL). Goldstein and Müller-Wieland (2016) reported that only 30% of the diabetic patients with type 2 can be treated with insulin injections and diet. Despite this treatment for type 2 DM, considering factors associated with medication, such as expense, bodily harm, means of treatment, reluctance to take medication and side effects, patients usually go back to using non-medicinal therapy (i.e. herbs). Thus, the traditional methods of therapy for type 2 DM are being revived as a means of healing the disease.

2.6. Risk Factors for type 2 Diabetes

There are many risk factors associated with type 2 Diabetes Mellitus, some of which are a result of modifiable environmental factors, such as obesity and physical activity (Bassuk and Manson (2005); Van Gaal et al.,2006), while others are linked to non-modifiable factors such as age, family history and genetics (Thayer *et al.,* 2010 ; Wass and Stewart, 2011). The following sections will present some of the links between these risk factors and diabetes. Although T2DM is more common among obese people (Horton (1990) and Franz *et al.,* 2015), it cannot be concluded that obesity causes diabetes as there are cases whereby non-obese people as well as some very obese people are not diabetic (Malik *et al.,* 2013; Horton (1990); Williams and Pickup (2004) have revealed that the relationship between obesity and diabetes depends mainly depends upon three factors: duration of diabetes and degree and distribution of obesity. Moreover, Franz *et al,* (2015) claim that obesity increases the risk of developing type 2 diabetes given an inherited propensity to develop the condition. This suggests that a person's genetic disposition is enhanced by environmental factors.

Some of the lifestyle modifications that developing countries, such as KSA have made, have resulted in a high-caloric food intake and a decrease in physical exercise. This in turn has led to an increase in Body Mass Index (BMI), which Malik (2013) found to be a reason that obesity is such a common problem. This is a major concern, as these lifestyle modifications have lead to an increase in the number of diseases (such as DM), which have caused higher death rates in such societies than before these lifestyle modifications were introduced (Boutayeb, 2005; Amuna and Zotor, 2008). In addition, Memish *et al.,* 2014 reported that one of the main reasons for the increase in serious illness and death in KSA is obesity.

Furthermore, a survey was conducted in the Kingdom of Saudi Arabia with the help of World Health Organization (WHO) in 2005, to measure the increasing obesity rate and associated factors causing the increased rated of DM. However there have been no further surveys conducted to check efforts to prevent obesity carried out by Saudi Ministry of Health (SMOH). Furthermore, Memish *et al*, (2014) reported the findings from a survey conducted by the

SMOH and the Institute of Health Metrics and Evaluation in 2013, which demonstrated that obesity levels in SA had significantly risen from the late 1980s to the mid1990s.

The report showed that the Saudi population had many health issues such as high blood pressure, diabetes and high cholesterol levels, all of which are associated with obesity. The report claimed that the increased rate of obesity among the Saudi population was due to the lack of physical activity and low consumption of fruits and vegetables. Wang and Beydoun (2009), agree with this claim as they found that an increased daily consumption of fruits and vegetables was often associated with a decreased risk of obesity. Furthermore, Camoes (2011) also found that the rate of obesity increases in men and women due to less physical activity.

Moreover, the Saudi Ministry of Health (SMOH) recognised that education is also an important factor that helps prevent obesity in those educated in SA. They identified the high risk groups as being old people, uneducated or inactive people. In addition, Gakidou (2014), claimed that the rate of obesity is higher in less educated people when compared to those who had received a higher level of education. It is for this reason that the SMOH monitored and regulated different health programmes, with the aim of decreasing overall obesity rates, by focussing on creating an awareness among the masses of the risk of diabetes, and trying to convince them to change their eating habits (MOH, 2012).

2.7. Lifestyle modification and Type 2 Diabetes

2.7.1. Dietary factors and type 2 Diabetes

A dietary plan prepared by a nutritionist could have a vital role in type 2 diabetic patients' management. As Mann and Truswell (2007) explained dietary modifications could manage the disease by improving the blood glucose levels and reducing complications. Thus, eating a balanced diet to help control blood sugar is a very important part for the management of type 2 diabetic patient, since extra intake of sugar could be harmful for the patient, so controlling the diet could be helpful in controlling diabetes (Whiting *et al.,* 2011).

Glycaemic Index (GI) provides an indication of the speed at which certain foods increase blood glucose levels after eating a meal. Foods that score 70 and above on the index are considered to have a high GI, and lead to a rapidly increasing blood glucose level. On the other hand, low glycaemic index foods range between 0 and 69, for which blood glucose levels rise slowly (Al-Mssallem, 2014). Foods lower on the GI have determinable benefits on glucose control and can improve metabolic control among type 2 diabetic patients by reducing chronic inflammation, improving lipid metabolism and insulin sensitivity (Kalergis, 2005 and Du *et al.,* 2008).

Figure 2.4 below illustrates the effect of the glycaemic index on blood glucose levels. The diagram shows that food with high glycaemic indexes (illustrated by the red line) caused a sharp increase in blood glucose levels after eating a meal. Following this, there was a rapid decrease in the concentration of glucose in the blood half an hour after eating a meal. On the other hand, the green line (representing low Glycaemic index foods) shows the blood sugar levels rising slowly and then falls gradually afterwards (Elwins, 2009).

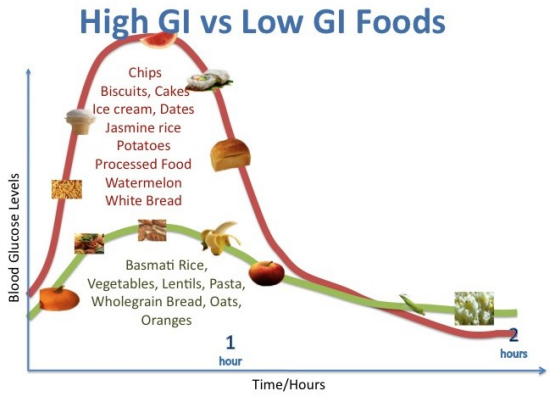


Figure 2.4.The influence of food that impact the GI on the blood glucose level (Kinshuck Diabetes Organisation ,(2014)

For this reason, Du *et al,* (2008) recommend low glycaemic index foods, such as fruits, vegetables, legumes, pasta, oats and rice, while restricting high glycaemic index foods, in order to control blood glucose levels among type 2 diabetic patients. The conclusions of later research by Al-Mssallem (2014) also recommend that Saudi's should be encouraged to follow a healthier diet by increasing the consumption of fruits and vegetables, which are rich in fibre. Generally, foods that are rich in fibre have a low glycaemic index, although certain foods that contain low amounts of fibre also have low glycaemic indexes. Furthermore, foods high in fibre that also have a low glycaemic index (as listed in table 2.3) tend to be absorbed slowly, thus having a fundamental effect on postprandial glucose levels. By reducing the absorption process, food remains in the intestine for more than two hours after eating a meal, which may help a diabetic patient feel fuller for longer (Al-Mssallem, 2014).

Moreover, Al-Mssallem (2014) reported that most of the traditional Saudi foods, such as rice, vegetables, whole grain, wheat and palm dates, ranged between moderate GI (>55 and <70) and low GI (≤55). As shown in Table 2.3, the GI for dates with Arabic coffee is 63, while the GI for dates with sour milk or yoghurt is fairly low at 29. Miller *et al*., 2003 found that dates with yoghurt have a beneficial effect on blood glucose levels due to the presence of protein and its effect on postprandial blood glucose levels. However, the findings of later research by Al-Mssallem and Brown (2013) suggest that consuming dates with Arabic coffee increases the blood glucose level rapidly due to the caffeine in the coffee.

Table 2.3.The Glycaemic index of food (Hamilton Health Science 2003)

Foods	Glycaemic index	Foods	Glycaemic index
Apple	37 GI	Yoghurt low fat	14 GI
Carrots	51 GI	Spaghetti	43 GI
Cashews	22 GI	Peanut putter	29 GI
Cherries	25 GI	White Rice	45 GI
Orange	44 GI	Kiwi fruit	50 GI
Skimmed milk	32 GI	Bananas	45 GI
Dates with Arabic Coffee	63 GI	Sweet potato	49 GI
Dates with sour milk or yogurt	29 GI	Lentils	26 GI
Pasta	32 GI	Dried apricots	31 GI
Low fat yogurt	14 GI	Lentil soup	44 GI
Baked beans	48 GI	Macaroni	45 GI

Mann and Truswell (2007) observed the relationship between food intake and the chances of developing DM and found that high starchy carbohydrate and sugary food consumption was the cause of a noticeable increase in the blood glucose levels of patients. Thus, they (ibid, 2007) claim that by having a balanced diet, the intake of natural carbohydrates such as legumes, wholegrain cereals and fruits could have a beneficial effect on glycaemic control, thus allowing diabetic patients to control their BGL. On the other hand, an unbalanced diet would mean an intake of high processed carbohydrates such as sugar, rice and flour, which could increase the BGL. Thus, by varying carbohydrate consumption, diabetic patients can control their blood glucose levels.

The amount of food intake increases in diabetes patients but the reason behind this action is still not understood and this is the main cause of obesity

in diabetics. It was also found on the basis of various experiments that high sugar consumption especially the complex sugar, sucrose, is not directly involved in causing this disease Mann and Truswell (2007). According to a few observations, it is deduced that nutritional intake directly affects the chances of diabetes in patients.

It is very important for a diabetic patient to increase the intake of fibre in their diet plans because dietary fibre is directly associated with blood glucose level and a patient's lipid profile. Velazquez-Lopez (2016) observed that patients with Type 2 diabetes can easily reduce their blood glucose level by including fibre in their diets, while also lowering the level of triglycerides and lipid in the human body. Thus, the high amount of fibre in a diet is directly proportional to low HbA1c, high HDL-c levels and a lower body weight (Velazquez-Lopez, 2016). In addition, Post *et al,* (2012) reported that dietary fibre was very helpful in lowering the blood sugar level in type 2 diabetes patients. Recent studies (Fujii 2013; Tanaka *et al.*, 2013 and Yang *et al.*, 2014) suggest that a high dietary intake of fibre had a strong link with the decline of HbA1c levels and reducing complications related to patients with type 2 diabetes, such as stroke (Post *et al.*, 2012).

Furthermore, Wycherley *et al,* (2010) recommend diabetic patients to follow a reduced-calorie diet in order to minimize the portion size of carbohydrate and increase the protein portion in order to control weight, blood glucose levels, HbA1c and blood pressure.

It is very important for Type 2 diabetes patients to adhere to their dietary plans along with physical exercises to control the glucose level in their blood. However (Evert *et al.*,2013) found that diabetic patients who followed the strict diet plans as a part of their daily routine treatment, showed a greater control over their BGL than patients who only did exercise to keep themselves fit and healthy. In relation to diet plans, Nowlin *et al,* (2012) reported that high dietary intake of carbohydrate decreased body weight, but had an insignificant change on BGL and HbA1c levels.

Furthermore, Ajala *et al,* (2013) found that when patients with type 2 diabetes followed a dietary plan (low CHO, high protein and low GI) for 6 months, it had a beneficial effect on controlling the risk of developing the complications associated with type 2 diabetes such as CVD, increasing the BGL.

Kratz *et al,* (2013) illustrated that there was a strong positive correlation between dietary intake of saturated fat and the development of complications such as dyslipidemia, obesity, high cholesterol level (HDL) and cardiovascular disease (CVD). On the other hand, Mann and Truswell (2007) found that a good source of fat such as polyunsaturated fats, had a beneficial effect on reducing the risk of CVD for diabetic patients. Saturated fatty acid are responsible for various heart diseases and overweight issues compared to polyunsaturated and monounsaturated fats (Velazquez-Lopez, 2016). Therefore, it is important for the healthy human body to consume poly and monounsaturated fats more than saturated fats to stay healthy (Kratz, 2013 and Velazquez-Lopez, 2016).

Fruit and vegetables are a rich source of flavonoids (Geissler and Powers, 2005). Khan (2014) reported that the dietary intake of food that is rich in antioxidants (phenolic content) such as black and green olives, dates, red grapes, pomegranate and ginger, have a beneficial effect on human health. Furthermore, fruit and vegetables are a good source of antioxidant vitamins (tocopherols, vitamin C, carotenoids), fibre, selenium, potassium, and folate (Mann and Truswell 2007). Foods rich in flavonoids and antioxidants had a beneficial effect on managing the vascular function in order to reduce cardiovascular diseases (CVD) (Geissler and Powers, 2005). Moreover, an increase in oxidative stress in the human body can lead to the development of several diseases such as cancer, CVD and inflammatory disease (Geissler and Powers, 2005). The dietary intakes of foods that are rich in flavonoids could reduce reactive oxygen, reduce the oxidative stress and reduce the prevalence of chronic diseases.

2.7.2. Physical activity and Type 2 Diabetes

Physical activity mainly affects the metabolism rate of glucose, which is why athletes have less glycaemia after a glucose load and insulin responses are diminished compared to untrained persons of similar weight (Knowler *et al.,* 2003). Conversely, profound physical inactivity such as bed rest is associated with the development of abnormal glucose tolerance and higher insulin levels **(**Ramachandran *et al.,* 2006). These observations suggest that physical activity influences insulin resistance (Kosaka *et al.,* 2005). There are few epidemiological studies that have established a relationship between T2DM and physical activity. For example, Lindström *et al.,* 2006) found that the prevalence of diabetes type 2, was twice as high in those with lower degrees of physical activity. While suggestive of a protective effect, the amount and degree of physical activity needed to achieve protection from diabetes is unknown.

Moreover, due to the lack of physical activity, Al Rukban (2003) claims that the Saudi youth is facing a problem with obesity. This association was true among men, but not women. Whereas men were almost equally distributed between all levels of physical activity, most women reported being inactive or having a low level of physical activity. According to Kriska (2003), physical activity (PA) is an important modifiable factor for type 2 diabetic patients in addition to a “diabetic diet” as it improves control of the complications associated with Type 2 diabetes. Furthermore, (Geissler and Powers, 2005) suggests that physical activity may also have a beneficial effect on blood glucose levels in Type 2 diabetic patients. Thus, making lifestyle modifications, such as increasing physical activity, could play an important role in controlling type 2 diabetes.

2.8. Control and Management of Type 2 Diabetes Mellitus

There are several ways in which type 2 diabetic patients can control their disease. These include giving up on, or reducing smoking habits; being active; following a modified diet; being willing to self-monitor their blood glucose levels regularly and adhering to treatment (Geissler and Powers, 2005). Moreover, larger institutions such governments, could also contribute towards the control and management of type 2 DM. Among the actions that they could be taken is providing an easy-to-follow health education programme for type 2 diabetic patients, which provides essential information that would help them control and manage their disease. Furthermore, health campaigns encouraging diabetic patients to reduce the amount of cigarettes they smoke gradually and eventually give up on smoking, could also contribute to a reduction in the risk of cardiovascular diseases (CVD), while clinical campaigns encouraging obese diabetic patients to change their lifestyle by losing weight, could also help to reduce the development of the disease (Mackay *et al.,* 2013).

2.9. Nigella sativa seeds

2.9.1. *Nigella sativa* seeds botanical information

The *Nigella sativa* plant comes from the *Ranunculaceae* family of herbs. For over two millennia the seeds have been made into herbal medicines and in a number of nations and the seeds are also used as a food flavour and additive (Zubaida *et al.,* 2001). *Nigella Sativa* seeds are also called black seeds as they are black in colour while triangular shaped, with one pointy smaller end (figure 2.5). The length of one of these seeds is one-eighth of an inch with a pure white and oily interior and gives off the smell of lemon and light carrot soupcon upon rubbing (Ahmad *et al,,*2013)

Figure 2.5. *Nigella sativa* seeds and plant flower (Al-Ghamdi, 2001 and ASSI *et al.,* 2016)

Nigella sativa seed is termed as the 'Habbatul barakah' in Arabic, translated as 'the seed of blessing' for the therapeutic potential it holds as a medicinal herb among the Arabians. Although the USA and Europe have only recently begun to learn about *Nigella sativa* and its benefits, the Middle East, Far East, Asia and Africa are well accustomed to the amazing curing ability of this organic regime. Records of different historical periods also reveal that *Nigella sativa* has been used as medicine benefits throughout history. For example, its use have been traced back to the ear ly Egyptian traditions where Tutankhamen's tomb was uncovered to hold *Nigella sativa*, which suggests that *Nigella sativa* was seen to be of value, since it was considered that objects found in the tomb of a ruler would help them in the life after death (Hussain and Hussain, 2016).

Furthermore, Hussain and Hussain (2016) have also found that for more than 4000 years the *Nigella Sativa* has been known all over the world. Among other organic compounds *Nigella sativa* seeds have also been mentioned in the religious traditions of the Islamic faith as being a cure for every illness except death **(**Hussain and Hussain, 2016). Therefore, this suggests that *Nigella sativa* seeds were used for their medicinal properties over 1400 years ago in the Middle East. With continuous intake of this seed, recent research that include Zubaida *et al.,* (2001); Fararh *et al, (*2004) Mohtashmi *et al.,* (2011); Hussain and Hussain (2016) suggests that this seed has an immense ability to enhance the biological immunity.

Many diseases such as bronchial asthma and bronchitis, rheumatism and similar inflammatory conditions have been treated with *Nigella sativa* seed with much anticipation in the Middle East and Far East countries for quite a while now (Mutabagani (1997); Al-Ghamdi (2001); Keyhanmanesh *et al.,* 2014). Among other functions this helps in boosting the release of nursing mother's milk, healing gastrointestinal problems, enhancing biological immunity, strengthen digestive ability and excretion and also counter parasitic infestation (Rajkapoor *et al.,* 2002 and Kanter *et al.,* 2005). The oil extracted from this seed is also used topically to heal flu symptoms and has also been used to cure skin ailments for example eczema and boils (Keyhanmanesh *et al.,* 2014).

2.9.2. Chemical composition and Nutritional value of *Nigella sativa* Seeds

Nigella sativa seeds are full of nutrients, organic compounds and minerals. According to Khan (1999), they contain traces of minerals, ash, fixed oil, moisture, Arabic acid, cellulose, albumin and other dissolvable substances as well as traces of oleic acid (acid value 30.30). El-shiekh (1999) ; Ramadan (2007), Keyhanmanesh *et al.,* (2014) ,Hussain and Hussain (2016), further found that these seeds are also made up of 18-21% protein, thus contain amino acids, as well as two kinds of fatty acids: saturated and unsaturated. Furthermore, Al- Jasser (1992) and Keyhanmanesh *et al.,* (2014) also found that *Nigella sativa* seeds have many other elements such as potassium; phosphorous, sodium and iron is present in abundance.

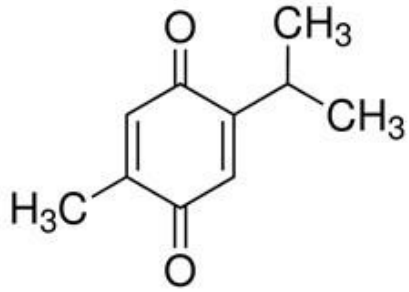


Figure 2.6. Bioactive compound Thymoquinone (TQ) from *Nigella sativa* extract. (Hussain and Hussain 2016)

According to Arora (2008), in the nutrition-rich seeds of *Nigella sativa* essential amino acids can be found as can carbohydrate, fat and vitamins as well as carotene, which the liver converts into vitamin A. Among other beneficial substances found within the *Nigella sativa* seed are potassium, iron and calcium.

Different specimens of *Nigella sativa* seed from various countries have been investigated and it has been observed that it has a great nutritional importance i.e. protein (~22%), fat (38- 40%) and carbohydrates (~32%) (Takruri and Dameh, 1998). Moreover, Hussain and Hussain 2016 reported that the *Nigella sativa* seed has carbohydrates (38%), protein (21%) and total fat (35%). *Nigella sativa has* rich source essential fatty acid (EFA) such as oleic, linolenic (polyunsaturated omega-3 fatty acid) and linoleic acids (polyunsaturated omega-6 fatty acid).

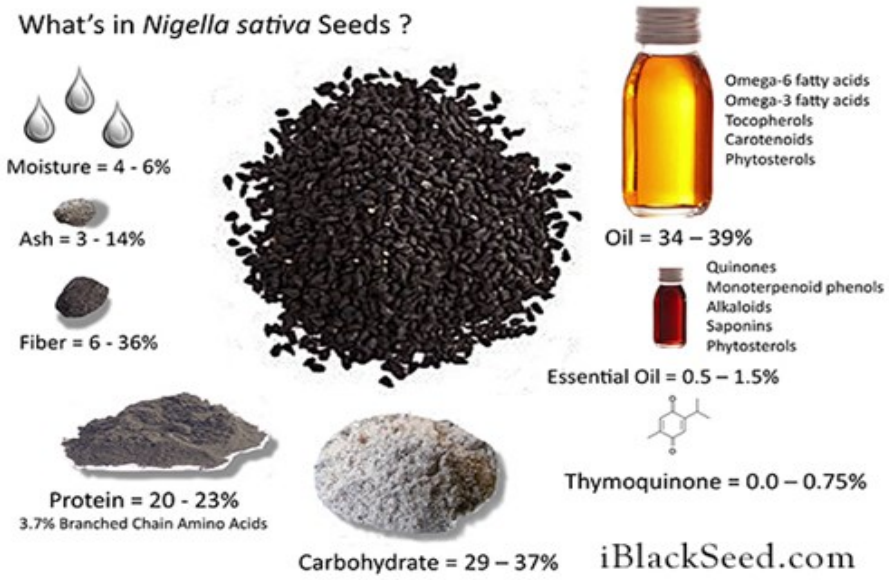


Figure 2.7. Nutritional facts for *Nigella sativa* seeds (Iblackseed.com)

The weight of the seed, according to its mineral and vitamin quantity, is made up of iron (105 mg) , copper (18 mg), zinc (60 mg), phosphorus (527 mg),

calcium (1860 mg) (Tekeli , 2014), thiamin (15.4 mg), niacin (57 mg), pyridoxine (5.0 mg) and folic acid (160 mg) (Takruri and Dameh (1998), Venkatachallam *et al.,* 2010). Furthermore, Meziti *et al.,* (2012) conducted an experiment, whereby he found the existence of sterols, triterpenes, tannins, flavonoids, cardiac glycosides, alkaloids, saponins, volatile oils, coumarins, volatile bases, glucosinolates and anthraquinones, and revealed the quality of *Nigella sativa* seeds along with many other Saudi Arabian herbs used in traditional therapy. In the same year, Gharby *et al.,* (2015) uncovered 67 compounds from the oil extracted from the *Nigella sativa* seed including monoterpenes (~46%); carbonyl compounds (~25%); phenols (~1.7%); alcohols (~0.9%) and esters (~16%). Gilani *et al,* (2004); Keyhanmanesh *et al.,* 2014.

Furthermore, Table 2.4 below shows the nutritional value of *Nigella sativa* seeds as found by recent studies mentioned in ASSI *et al,* (2016).

Table 2.4.The Nutritional value of *Nigella* seeds (ASSI *et al.,* 2016)

General Nutritional information (Al-Ghamdi 2001)	**Protein**	**16- 19.9 %**
	Carbohydrates	33.9%
	Fiber	5.5%
	Water	6%
	Fixed oil	32- 40 %
	Volatile oil	0.4 – 0.45 %
Vitamins (Zahoor et al 2004)	Thiamine	15 µg/g
	Riboflavin	1 µg/g
	Pyridoxine	5 µg/g
	Folic Acid	610 I.U/g
	Niacin	57 µg/g
Minerals Contents (Zahoor et al 2004)	Calcium	1.859 mg/g
	Phosphorus	5.265 mg/g
	Iron	105 µg/g
	Copper	18 µg/g
	Zink	60 µg/g

Gram (g)Micrograms (µg), milligrams (mg)

2.9.3. The General benefits of *Nigella sativa*

Nigella sativa seeds are widely used in the Middle East and Asian countries, are used as a good treatment for coughs and very effective when used with honey in the early morning on an empty stomach to stimulate the hunger

enzymes (ibid, 1987). Gilani*et al.,* (2004) also found that they can be used in medicines to treat different diseases such as fever, cold, headache, asthma, rheumatoid and other ailments of stomach and intestines.

Nair (1991) tested the effect of *Nigella sativa* seeds oil extract on mice and found that it was an effective antioxidant, which reduces the toxic effects of anti-cancer medicines and helps to maintain the haemoglobin and white blood cell count.

The biological resistance on hamsters is held up mainly through immunity and sustained cellular structure. The physical well-being and the performance of a body are made better. *Nigella sativa* enhances this course of action through triggering macrophage phagocytic effects through lymphocyte stimulation or directly. The hypoglycaemia and enhanced immunity of the biological system in rats due to the decreased liver gluconeogenesis is a conclusion of this ability (Fararh*et al.,* 2004). Lymphocyte counts and allergic ailments have been treated through this. (Kalus*et al,* 2003)

These previous in-depth studies on animals examined the effect of Ns in supporting the immune system and glucose levels. However, these animal studies were limited in how possible it is to extrapolate these findings to humans.

Furthermore, Mohtashami*et al.,* (2011) claim that traditional medicine has made use of a number of different mixtures made with *Nigella sativa* seeds for the prevention and the treatment of not only diabetes but also a large variety of other illnesses such as blood pressure. In contrast, despite Mohtashami *et al.* (2011) showing a positive effect of NsO on fasting blood glucose in healthy adults, the study did not include diabetic patients. It could be that the reduction in fasting blood glucose with NsO works only with healthy participants.

The *Nigella sativa* seeds oil has a beneficial effect on back pain, skin and suitable for rheumatoid Mutabagani (1997) and AL-Ghamdi (2001).

ader*et al.,* (1993), Alimohammadi*et al.,* (2013) and keyhanmanesh*et al.,* (2014) mentioned that the reduction in the blood glucose levels with a *Nigella sativa* treatment caused by insulinotropic properties and decreasing of hepatic gluconeogenesis.

Bamosa *et al*. (2010), agreed with the previous study (Al-Hader *et al*., 1993) that showed a marked effect of *Nigella sativa* on blood glucose levels in alloxan diabetic rabbits, and also agreed with Labhal et al. (1997), who found an effect of Ns in controlling glucose homeostasis among sand rats.

In 1987, Al Awadi *et al.* published a paper in which they demonstrated that there was no hypoglycaemic effect of *Nigella sativa* in streptozotocin diabetic rats. Furthermore, in 2004, Le *et al*. reported that Ns has no effect on glucose levels in normal rats. The different results for these studies could be due the different ways of extracting the *Nigella* seeds or to the different animal species.

2.9.4. Effects of *Nigella sativa* on Diabetes and Blood Glucose

Globally, millions of individuals suffer from the chronic illness of Diabetes Mellitus (DM), which has resulted in an interest in research into the factors that could help to treat the disease. In the late 1900s studies were carried out to test the effect of *Nigella sativa* (Ns) on various diabetic animals. Therefore, keyhanmanesh*et al.,* (2014) suggested that plants such as Ns could be used to control diabetes. Furthermore, Al-Hader*et al,* (1993) also found a significant effect of the volatile oil of Ns seeds on insulin levels in diabetic rabbits, implying that Nscould be used as a treatment for hypoglycaemia.

The few animals studies support the hypothesis of this thesis and also the clinical studies in humans sitting support the gap that using NS has a positive effect on blood glucose levels (see table 2.5). Furthermore, the clinical trial showing these results in humans has a robust study design and the literature review shows that there are mixing terms of animal outcomes and human outcomes.

Although studies on animals may provide an indication as to what kind of an effect a particular substance (in this case Ns) would have on humans, the findings of such studies can be considered problematic when trying to understand the effect of Ns on humans, especially because the biological functions of the animals used were very different from that of human beings (Tekeoglu*et al.,* 2007).

However, another way in which an understanding of the effect of Ns on

humans can be achieved is through the commonly used folk remedies. Although folk remedies and medical alkaloids have often been successful in healing different diseases, they are not based on any scientific findings. Despite this fact, the ingredients used within folk recipes and regimens (such as Ns) do provide an interesting subject for scientific research as it could help to develop an understanding of the beneficial healing ability of Ns and why it has been used as an effective treatment for many diseases (including DM) throughout history (Tariq, 2008; Ahmad *et al.,* 2013).). In addition, Rchid*et al*, (2004) discovered that traditional Moroccan treatments for DM also made use of Ns, while Mohtashami*et al,* (2011) also suggests that to treat and prevent diabetes and a large variety of other illnesses, traditional medicine has made use of a variety of *Nigella sativa* seed concoctions.

Such findings lead to a series of controlled clinical studies whereby the effect of Ns was observed in humans. For example, Bamosa*et al*, (1997) gave healthy adults 2g/day of Ns seeds for 2 weeks and found a reduction in BGL. Bamosa*et al*, (1997) started with a small group, healthy students and for a short duration, because further research was needed to investigate the actual reduction in blood glucose levels. Further research then included patients with T2DM, such as the study of Bilal *et al*., (2009), who used a dose of 0.7g/day of Ns seeds for 40 days, and noticed a highly significant reduction in FBG levels on Type 2 diabetes patients. Furthermore, in a study by Bamosa*et al,* (2010) sufferers of Type 2 DM were given different doses of *Nigella sativa* seeds (1, 2 and 3g/day) as a complementary treatment to their existing anti-diabetic drugs, to investigate the impact of *Nigella sativa* seeds on the glycemic control. Despite Bamosa*et al*, (2010) having improved their study since 1997 with a time duration of consuming the *Nigella sativa* seed powder to 3 months, however, still there is a limitation that the unspecific selection of the diabetic patients. Because of that, in 2015, Kaatabi *et al*. designed a study to compare their results with Bamosa *et al*., 2010. Therefore, the improvement in BGL levels were reduced over one year after using NS seeds powder 2g /day. The inclusion criterion was HbA1c > 7% and < 9%. The good effect of using 2g/day of NS powder was that of enhancing the antioxidant defence system for T2DM.

Kaatabi *et al*. (2015), have illustrated that *Nigella sativa* seed powder (2g a day) has postive effects on fasting blood glucose and HbA1c levels. In Kaatabi's et al. study, there was no specific diet to follow for the diabetic patients and they also did not use physical activity diaries because the study was over a long period.

Although the factors measured all indicated a decrease in BGL, when 1g of *Nigella sativa* was ingested daily, the results were statistically insignificant. These results remained the same when 3g of the seed powder was ingested daily. The different doses of *Nigella sativa* powder administered in the research resulted in no negative effects in terms of the kidney or hepatic functions of the study subjects. Therefore, Bamosa*et al*, (2010) concluded that an intake of 2g of *Nigella sativa* seeds daily for 12 weeks, reduced BGL levels in Type 2 diabetic patients. The reduction in blood glucose level could be possible due to the reduction in gluconeogensis (GNG) in the liver. Thus help to avoid hypoglycemia in type 2 diabetes. It has been found that increasing the hepatic glucose production could increase the fasting blood glucose by increasing the GNG for diabetes patients. Bamosa 2010

Two years later, another similar study was conducted by Najmi*et al,* (2012) to evaluate the effect of Ns seeds on fasting blood glucose (FBG), 2 hours postprandial (2hPP) blood glucose and glycated haemoglobin (HbA1c) in patients with poor glycaemic control. The results indicated that treatment with Ns significantly decreased the FBG, 2hPP blood glucose and HbA1c after 2 months, which would be considered an improvement in glycaemic control for patients with Type 2 diabetes.

Moreover, some studies extended the research of Ns by extracting oil from the seeds (NsO) and investigating the effect it had on humans. For example, Mohtashami*et al,* (2011) found a statistically significant correlation between the ingestion of NsO and a reduction in fasting blood glucose levels of healthy adults. Furthermore, Hosseini *et al,* (2013) conducted a randomised trial of Type 2 diabetes patients in Iran, to investigate the effects of NsO on glycaemic status (FBG, PPBG and HbA1c), lipid profile, renal function and BMI. They (ibid, 2013) concluded that a dose of 5ml/day of NsO for 3 months, seemed to

improve glycemic control and BMI, while also observing a significant reduction in FBG, 2hPP blood glucose, HbA1c and BMI. Hosseini's *et al* (2013) study has the weakness of not showing clearly how the data were handled. However, the data collection methodologies were presented in detail. Heshmati *et al,* (2015) also found that NsO caused a significant change in glycaemic profile (fasting blood glucose FBG, glycated haemoglobin HbA1c) after carrying out a study to investigate the effects on glucose metabolism in patients with Type 2 diabetes. They (ibid, 2015) examined males and females aged between 30-60 years old, who received *Nigella sativa* oil (NsO) 3g/day (of soft gel capsules) for 12 weeks and suggest that a diet supplemented with NsO may help to control glycaemic profile of T2DM patients. Hishmati *et al* (2015) discussed the findings from pervious research such as Bamosa *et al (2010)* and found that their findings concurred.

2.9.5. *Nigella sativa* seeds on Blood Pressure and Antioxidants

There have been several studies reporting the effe ct of *Nigella sativa* on Blood Pressure (BP) and artery disease**.** For example, Najmi *et al,* (2007) carried out a numerical study of the beneficial effect of *Nigella sativa* oil (NsO) on parameters of metabolic syndrome in patients with Type 2 diabetes, and showed that there was a significant change in BP as a result of a dose of 5ml/day for 6 weeks. This study demonstrates particular strength in the selection and allocation of study participants.

One year later, Dehkordi and Kamkhah*,* (2008), investigated the antihypertensive effect of *Nigella Sativa* seeds extract in Type 2 diabetic patients. In this study, the patients consumed 200 mg and 400 mg of NS/daily for 8 weeks and this resulted in a significant decline ($p<0.05$) of the systolic blood pressure (SBP) and diastolic blood pressure (DBP), when compared to the baseline after 2 months. Dehkordi and Kamkhah's study selected suitable participants according to the inclusion criteria and presented their methods clearly.

Five years after their study on NsO, Najmi *et al,* (2012) conducted another study whereby they measured the impact of 500mg/day of *Nigella Sativa* seeds on the BP of patients with metabolic syndrome over a period of 8 weeks.

BP measurements were taken at the baseline and then again at 2,4,6, and 8 weeks. They (ibid, 2012) found a significant decrease in SBP, DBP, which they attributed to the antihypertensive effect of Ns.

Furthermore, Fallah Hosseini *et al,* (2013) examined the effect of *Nigella sativa* seed oil (NsO) on SBP and DBP in healthy participants with a dose of 5ml daily during an 8 week period, and found a significant decline in both parameters (SBP and DBP) when compared to the placebo and baseline groups. They claimed that one of the reasons for the beneficial effects of *Nigella Sativa* on blood pressure was due to the lowering of arterial pressure (AP) and heart rate. (Eltahir *et al,* (1993); El Tahir and Ageel (1994), Fallah Hosseini *et al,* 2013). Fallah Hosseini's study discussed and analysed their data clearly and in detail.

Fallah-Hosseini*et al*, (2013) also suggest that another possible reason for the decrease in BP was due to the effect of *Ns* volatile oil, which contained unsaturated fatty acids, such as oleic and linoleic acids (Ghosheh *et al,* (1999) and Dogan*et al.,* 2010), and flavonoids, which could have been the cause of a drop in the arterial pressure and heart rate. Earlier studies (e.g. Takeuchi *et al.*, 2007; Miura *et al.*, 2008 and Medina Remon*et al.*, 2011), demonstrate that there is link between dietary oleic and linoleic acids intake and blood pressure. Furthermore, Fallah-Hosseini*et al*, (2013) also support the findings of Khattab and Nagi (2007), who suggested that the decrease in BP may also have been caused by thymoquinone, one of the antioxidant active components found in NsO.

Moreover, Galleano *et al,* (2010) explain that NsO is a rich source of polyphenols and flavonoids (a part of a phenolic family of compounds that have antioxidant properties), which are important in antioxidant activity and free radical properties. Carr and Frei (2000) and Fallah-Hosseini*et al*, (2013) claim that it is these properties within NsO that cause a decline in the BP levels, which in turn leads to a decrease in the oxidative stress.

Inhibit the oxidative stress by antioxidants activity and free radicals participating in impaired endothelial function are risk factors for hypertension (Carr and Frei ,2000; Fallah-Hosseini*et al,* 2013) And the treatment with NsO

decreased the BPs was due to antioxidant activity of thymoquinone against l-Name- induced hypertension (Kattab and Naqi 2007; Fallah-Hosseini*et al,* 2013) *Nigella sativa* is a rich source of antioxidants and flavonoids and polyphenols

Nigella Sativa improve glycaemic control and Kaatabi *et al,* (2015) suggested that long duration of using NS supplementation as a treatment for diabetic patients will improve glucose homeostasis and raised antioxidant defence system in Type 2 diabetes patients.

2.9.6. Effect of *Nigella sativa* on Cholesterol Levels

Very few studies have been carried out to investigate the effect of Ns on cholesterol levels, and the studies that have been carried out in this area are mainly on animals. For example, Zaoui *et al*, (2002) tested *Nigella sativa oil* on diabetic rats and the effect it had on cholesterol levels over 12 weeks, and observed a decrease in the cholesterol level. Zaoui's *et al* study has been shown a weakness in investigating the *Nigella sativa's* effects only in diabetic rats and mice with no tests performed in control animals.

Furthermore, Dahri*et al,* (2005) conducted a study on 24 eight-week old albino rats and observed the level of cholesterol after administration of Ns. Upon initiating the experiment, blood tests of the rats were taken, in order to measure cholesterol levels, and for 20 weeks they were given specific control and experimental nutritional regime. From this experiment it was concluded that serum HDL was elevated and LDL cholesterol was reduced.

Kaatabi *et al,* (2015) undertook one of the few studies on humans (diabetic patients) to investigate the effect of *Nigella sativa* powder on lipid profile levels and showed a substantial reduction in cholesterol level, following an intake of 2 grams of *Nigella sativa* powder daily for 12 weeks. The limitation of Kaatabi's *et al* study was that all patients were not following a specific diet and making physical activity records. However, these limitations had only a slight effect on the study. A strong point was presenting the supporting information in tables and figures.

Summary

Traditional Arab treatments of biological ailments have always originated from herbs. During experimental studies very few herbs have been investigated for the potential treatment of diabetes and those that have been carried out have based their findings on animal studies. Hence it has been concluded that traditional herbs that possess anti-diabetic effects may prove to be beneficial for individuals suffering from diabetes along with other hypoglycaemic medicines.

Many experiments still have insufficient statistics, leading to disarray in the findings such as small sample size, decrease time of experiment, placebo group and lack of authority on subject. Hence, considering the lack of quality data and inference it is too early to assess and give a remark to the herbs with anti-diabetic potential.

As shown in table 2.5 below, the previous intervention studies on human have highlighted a potential effect of *Nigella Sativa* seeds supplemented in diabetes Type 2. In addition, *Nigella Sativa* different types (oil, powder, extract and seeds) have a beneficial effect on blood glucose and improving glucose profile. In this study, it has been chosen *Nigella sativa* as a raw seeds because the other researchers have further examined the Ns as oil, powder and as a tea. There is a need for more research on Ns as a raw seeds it's self. The methodologies of clinical trials (Randomised clinical trial, clinical trial, Double blind and Randomised clinical trial) could have influenced the results obtained (see table 2.5).

Table 2.5. Summary of the studies for *Nigella sativa* seeds

Study paper	Study population N=Sample Size	Inclusion criteria	Study design	Period of intervention study	Type and dose of NS	Outcome and Association (+P Value)
Bamosa *et al.,* 1997	{N=16 9/6}	Second year male medical students Saudi Arabia	Clinical trial	2 weeks	NS 2g/day	Sig change in FBG and TC (P<0.05) No significant decrease in TG (P>0.05)
Najmi *et al.,* 2007	{N=161 80/81} 40 – 60 years	Metabolic Syndrome North India	Randomised clinical trial	6 weeks	NSO (Extracted oli) 5ml/day	Sig change in FBG, HDL and LDL (P<0.05) No significant decrease in Weight, BP, (P>0.05)
Dehkordi and Kamkhah , 2008	{N=108 36/39/33} 35 – 50 years	Hypertension's patients	Double blind and Randomised clinical trial	8 weeks	Extract of NS (Extracted by water) 200 mg/day 400 mg/day	Sig decrease ↓SBP and DBP (P<0.05) No significant change in weight, TG and HDL(P>0.05)

Najmi *et al.,* 2008	N= 60 30/30	North India	Clinical trial	6 weeks	5 ml /day NSO (Extracted oli)	Sig reduction in FBG and Lipids and TC(P<0.05) Non sig TG, HDL and WC (P>0.05)
Bhatti 2009	N= 10 50 – 55 years	Hyperlipidemic patients Pakistan	Controlled trial, Non control	2 months	1g/day	Sig change in TG, TC, LDL and HDL (p<0.05)
Bilal *et al.,* 2009	N=41 30 – 60 years	T2DM Pakistan	Controlled trial, Non-control	40 days	NSO (Extracted oli) 0.7 g/day	Sig. decline ↓FBS (P<0.001)
Qidwai *et al.,* 2009	{N=73 39/34} ≥18 years	Pakistan	Double blind and Randomised clinical trial	6 weeks	1g/day	No significant change in FBG, BMI , BP and Lipid profile (P>0.05)
Bamosa *et al.,* 2010	{N=68 23/26/19} 18- 60 years	T2DM KSA	Controlled trial, Non- control	3 months	NSP (powder) 1,2 and 3g/day	Sig reduction in FBG, 2hPPBG, HbA1c (p<0.05)in group 2.3g/day No significant change in group 1g/day (P>0.05)

Datau *et al.,* 2010	{N=39 19/20) 30 – 45 years	Obese Men (Indonesia)	Double blind and Randomised clinical trial	3 months	NS 1.5g/day	Sig reduction in weight and WC (P<0.001) No significant change in BP, FBG, HDL and TG (P>0.05)
Haque *et al.,* 2011	{N=60 30/30} 40 – 60 year	Anti-obesity therapy in Metabolic syndrome North India	Randomised clinical trial	6 weeks	NSO (Extracted oli) 5ml/day	Non Sig in weight and WC
Ibrahim *et al.,* 2011	N=18 23- 31 years	Yemen	Controlled trial, Non-control	2 weeks	500 mg/day	Sig reduction in FBG (p<0.05) No significant change in Lipid profile (P>0.05)
Mohtashami *et al.,* 2011	{N=70 35/35} 25 – 60 years	Healthy adults (Iran)	Randomised clinical trial	2 months	NSO (Extracted oli) 5ml/day	Sig change in FBG, 2 and HbA1c (P<0.05)

Ahmed *et al.,* 2012	{N=66 41/25}	T2DM Egypt	Clinical trial	6 months	NS tea bag 5g/day Extract of N.Sativa)	Sig change in FBG, TC, LDL, TG and HDL (P<0.001)
Elrehany *et al.,* 2012	{N=55 40/15} 35 – 65 years	Patients with coronary artery disease and dyslipidemia Egypt	Clinical trial	8 weeks	NSO (Extracted oli) 900 mg/day	Sig change in BP, LDL, TG, TC and HDL (P<0.001)
Kaatabi *et al.,* 2012	{N=71 23/26/22} 18 – 60 years	T2DM KSA	Controlled trial, Non-control	3 months	NSP (powder) 1,2 and 3g/day	Sig reduction in TC, TG,LDL and HDL (p<0.05)in group 2.3g/day No significant change in group 1g/day (P>0.05)

Najmi *et al.,* 2012	{N=80 40/40} 40 – 60 years	Patients with poor glycemic control (North India)	Randomised clinical trial	8 weeks	NS 500 mg/day	Sig decreased in FBG, 2hPPBG, HbA1c and LDL(P<0.001) No significant change in TG and HDL (P>0.05)
Sabzghabaee *et al.,* 2012	{N=74 37/37} ≥18 years		Randomised clinical trial	4 weeks	NS 2g/day	Sig decreased in TC, LDL and TG (P<0.001) No significant change in FBG and HDL (P>0.05)
Shah *et al.,* 2012	{N=159 80/79} 40 – 60 years	Metabolic Syndrome Pakistan	Clinical trial	6 weeks	NS 500 mg/day	Sig change in FBG, HDL and LDL (P<0.05) No significant decrease in TG , TC, BP and weight (P>0.05)
Fallah Hoseini *et al.,* 2013	{N=70 35/35} 34 – 63 years	Healthy adults (Iran)	Double blind and Randomised clinical trial	8 weeks	NSO (Extracted oli) 5ml/day	Sig change ↓SBP and DBP (P<0.001)

Hoseini. *et al.,* 2013	{N=70 35/35} 34 – 63 years	T2DM Iran	Double blindand Randomised clinical trial	3 months	NSO (Extracted oli) 5 ml/day	Sig reduction in FBG, 2 hPPBG, HbA1c , BMI and TC (P<0.05) No significant change in HDL, TG and LDL(P>0.05)
Najmi *et al.,* 2013	{N=90 45/45} 40 – 60 years	Metabolic Syndrome North India	Randomised clinical trial	8 weeks	NS 500 mg/day	Sig decreased in SBP and DBP (P<0.001)
Ibrahim *et al.,* 2014	{N=37 19/18} 50 – 55 years	Menopausal women Malaysia	Randomised clinical trial	2 months	NS 1g/day	Sig decreased in TC, TG, FBG and LDL(P<0.05) No significant change in BP and HDL (P>0.05)
Kaatabi *et al.,* 2015	N=114	T2DM	CT	12 months	NS 2g/day	↓ FBG ↓ HbA1c

2.10. Ajwa dates

2.10.1. History of Ajwa dates

Dating back to 5000 BC, and cultivated only in Al Medina Al-Munwarah, Saudi Arabia, the Ajwa date is a staple of Middle-Eastern cuisine and diet. During the course of Ramadan, Muslims all over the world, break their fast with the Ajwa date. High in natural fibre, with a soft, fine texture (Khalid *et al.,* 2017), Ajwa dates provide a suitable amount of roughage to assist the ingestion process and maintain the balance of the digestive tract, whilst the high potassium content preserves and controls muscle contractions. Another key facet of Ajwa dates is the high iron content, which assists in the treatment and prevention of anaemia by increasing red-blood cell production (Ragab *et al.,* 2013). Ajwa dates are also hugely beneficial throughout the maternity process; in enhancing the breast milk in lactating women, children are less susceptible to disease and infection through the consumption of Ajwa-enriched milk, than normal breast milk (Ragab *et al.,* 2013).

Originating in Saudi Arabia, Ajwa dates are among the most costly dates available, costing approximately 80SR, £16 and $21 for one kilogram. They are found in the Madinah region of Saudi Arabia and characterised by their softness, dryness and high cost. Health experts in Saudi Arabia claim that Ajwa dates contain anti-oxidant elements due to the flavonoid glycosides found in them, thus they have antioxidant and anti-inflammatory effects (Assirey, 2015). Furthermore, a cyclo-oxygenase inhibitory effect, comparable to that produced by anti-inflammatory medications such as ibuprofen, celebrex, aspirin and naproxen, has also been found to be produced by Ajwa dates (Zhang *et al.,* 2013).

Moreover, fruits dates are certified as low in glycaemia on the glycaemic index as they have a value lower than 55, and a range between 29 and 55 (Al-Mssallem. 2014). This index highlights a food's capacity to increase blood sugar in relation to the carbohydrates present in the food. Such a trait increases the control of both lipids and glycaemia and is considered desirable as there is a correlation between a low glycaemic index and the diminished prevalence of cardiovascular disease, weight loss and diabetes. Whilst there is a considerable range witnessed in the glycaemic index of dates, and thus some dates are more

effective than others, Ajwa dates, in particular, are incredibly beneficial for the maintenance of the human body (Miller *et al.*, 2002 and Alkaabi *et al.,* 2011). Al-Khayri *et al.,* 2015 described the Ajwa date as a medium size and the colour of Ajwa is dark and should be consumed at tamar stage. There are 5 stages that take place over 7 months (see figure 2 .8below) for the growth of dates. Figure 2.9 (below) shows each of the stages of the ripening process from Hababouk to Tamar. The softness, flavour, colour, appearance and nutritional value of the dates is dependent on the stage at which it is used. The Ajwa date is picked during the tamar stage, which results in a variation in its chemical composition and a reduction in the nutritional value (Al-Shahib and Marshall, 2003 and Fadel *et al*., 2006).

Figure 2.8. Dates stages (Baliga *et al.,* 2011)

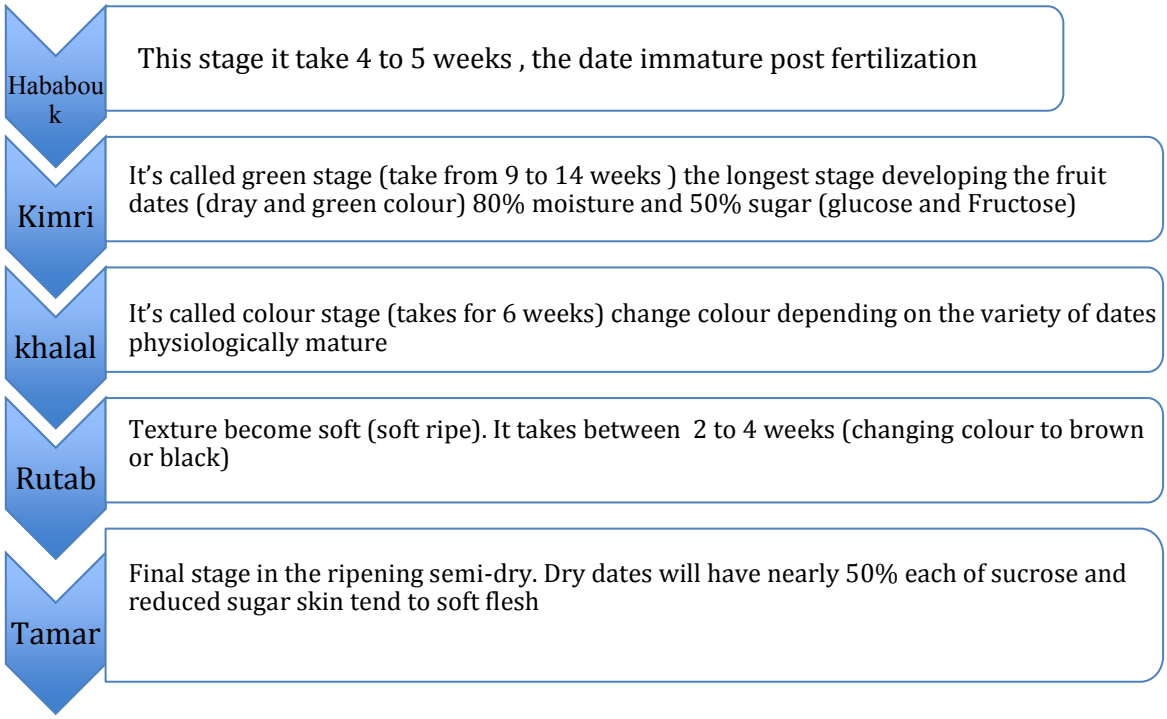


Figure 2.9. Date growing stage (Baliga *et al.,* 2011)

2.10.2. Chemical composition and Nutritional facts of Ajwa dates

Contemporary medical practice affirms that Ajwa dates aid in the prevention of cancer of the abdomen (Khalid *et al.,* 2017). Ajwa dates contain a wider range of elements than other dates and consist of: calcium, sulphur, oil, iron, phosphorous, manganese, potassium, magnesium and copper(see table 2.6).They are nutrition-rich and are made up of 60% sugar and 2% each of fat, minerals and proteins . (Hasan *et al.,* 2010).

The Ajwa date is one particular fruit that has a significant presence of polyphenolic such as (.Rutin 0.65 to 0.85 mg/100 g , Catachin 0.73 mg/100g and Caffeic acid 0.57 to 1.84 mg/100(Saleh et al., 2011; Hamad et al., 2015; Ahmed et al., 2016). In addition, Ajwa date has 283.43 milligrams of polyphenol per 100 gram serving. As a result, Ajwa dates are a key in the treatment of blood-related diseases. The presence of polyphenol compounds has a beneficial effect on glucose and lipid metabolism. (Jung *et al.,* 2006).

Table 2.6. The composition for Ajwa dates (*Phoenix dactylifera* L) (per 100 g) (Assirey 2015)

	Ajwa date
Sugar content of date flesh from cultivars (g/100 g dry weight).	
Ash	3.43 ± 0.01
Lipid	0.47 ± 0.001
Protein	2.91 ± 0.02
Moisture	22.8 ± 0.1
Total sugar	74.3 ± 0.2
Reducing sugar	71.1 ± 0.5
Sucrose	3.2 ± 0.03
Glucose	51.3± 0.3
Fructose	48.5 ± 0.2
Minerals composition of date flesh in four cultivars (mg/100 g dry weight).	
Calcium	187 ± 0.5
Phosphorus	27 ± 0.1
Potassium	476.3 ± 0.4
Sodium	7.5 ± 0.1
Magnesium	150 ± 0.7

Assirey (2015) and Khalid *et al,* (2016) reported that Ajwa dates are a rich source of dietary fibres, which are vital for the wellbeing of humans. An increase of an intake of dietary fibre could lead to a decrease in the cholesterol level, constipation and cancer. The Total Dietary Fibre (TDF) in Ajwa date stone was higher (26.4 to 33.9%) than the flesh of the Ajwa dates flesh (6.2 to 8.9%).

In addition, the Soluble Dietary Fibre (SDF) for the Ajwa date stone was between 13.5 to 22.5% and for Ajwa date flesh was between 6.2 to 13.5%,

whereas the Insoluble Dietary Fibre (IDF) for the Ajwa date flesh was 3.2 to 4.6% and 11.2 to 12.8% for the Ajwa stone.

Moreover, several studies (such as Al-Laith, 2009; Amoros *et al,* 2009; Al-Turki *et al*, 2010) have found that Ajwa dates are rich in polyphenols that are important in controlling cholesterol levels, which in turn decreases the chance of suffering from cardiovascular related diseases. Furthermore, Saleh *et al* ,(2011) mentioned that there are different values of the total number of polyphenols of the Ajwa date when compared to Sukkari and Khalas dates. They (ibid, 2011) found that Ajwa dates had a water extract of 455.88mg/100g, while Sukkari dates contained 377.66mg/100g and Khalas dates had 238.54mg/100g. Therefore, Ajwa dates had the highest value for the total amount of polyphenols. Hamad *et al*, (2015) and Saleh *et al,* (2011) explain that the reason for this is due to polyphenol concentration values varying depending on the method of extraction and how ripe the dates are **(**see table 2.7). Thus, the polyphenol value for Ajwa dates extract by aqueous was higher than alcohol.

Table 2.7. The Ajwa date contain higher polyphenol content (Eid *et al.,* 2013,Khalid 2016)

Dates growing stages	**Polyphenol content**
Kirmri stage	290 mg/100 g
Khalal stage	150 mg/100g
Rutab stage	20 mg/100g
Tamar stage	10 mg/100g

Ajwa dates are a type of fruit date palm (*Phoenix dactylifera),* which are a rich source of vitamins and minerals (iron, potassium, zinc, selenium and magnesium)(Ahmed *et al.,* 2014). An Ajwa date provides essential amino acid as shown in table 2.8 and are also rich in iron, which is important for people with anemia. Further benefits of the Ajwa date is that it has been shown to enhance hemoglobin levels. (Alghamdi, 2017).

Based of the varieties of nutrients present in Ajwa dates, recently many studies have used *Phoenix dactylifera* as a traditional medicine for treatment as it plays an important role in anti-diabetic activity

Table 2.8. Amino acid content of Ajwa date flesh (mg/100 g dry weight). Assirey (2015).

Amino acid (mg/100 g)	**Ajwa Dates**	**Amino acid (mg/100 g)**	**Ajwa Dates**
Aspartic acid	186	Valine	65
Glycine	83	Leucine	57
Histidine	26	Arginine	93

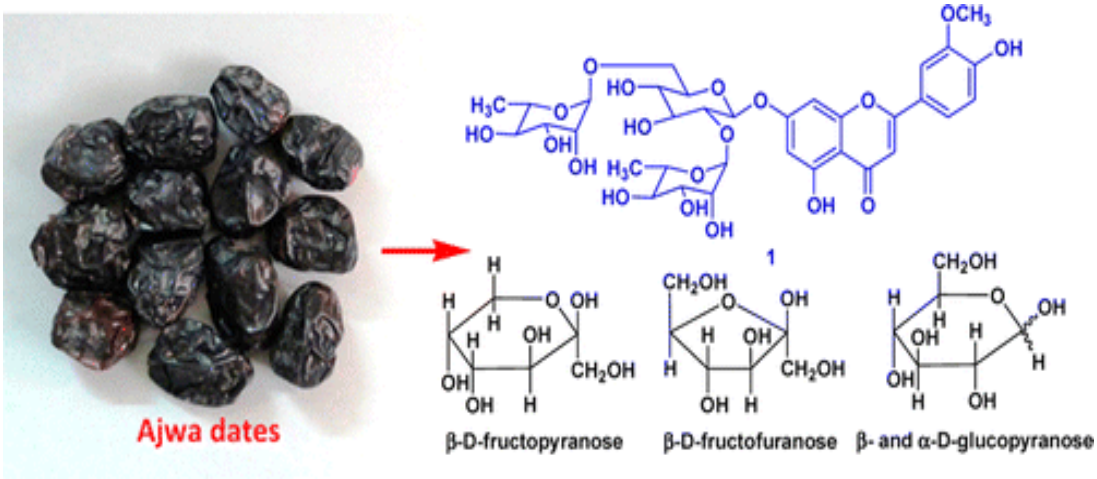


Figure 2.10. The chemical composition of Ajwa dates

2.10.3. Ajwa dates and antioxidants

Khalid *et al* (2017) evaluated a number of preclinical studies and reported that a dietary intake of Ajwa dates acts as a treatment for several illnesses such as (chronic disease and cancer) due to the presence of strong antioxidant, antimutagenic and hepatoprotective properties in the Ajwa date.

Moreover, Ragab *et al* (2013) conducted a study from Al-Medina Al-Munawarah and focused on the significant attributes of the Ajwa extract, in particular as an antioxidant and its tissue protection abilities. They (ibid, 2013) found that Ajwa dates possesses significant antioxidant properties that assist in reducing and restricting lead-induced transitions in oxidative biomarkers in serum. The reason this occurs remains uncertain, but polyphenols, flavonoids and flavones are all offered as suitable solutions, as they exist in the Ajwa date (Ragab *et al.,* 2013).

Several studies including Hasan *et al* (2010); Baliga et al (2011) and Hamad *et al* (2015) have found that tissue protection is afforded through 'free-radical scavenging' and the antioxidant aspect of the Ajwa date. They also found that the antioxidant nature of the extract from medicinal plants reduces the effects of metal toxicity – an aspect that is increasingly studied by researchers of phytotherapy. As a result, the extract could be used as a management tool in nutritional protocols surrounding lead poisoning. Ragab *et al* (2013) suggest that it is important to further elucidate the effects of the Ajwa extract, in order to fully comprehend the preventive and therapeutic benefits. Ragab's *et al* study however, was designed to study animals and therefore cannot be compared to results in humans.

2.10.4 Ajwa dates and Diabetes

The present treatments for Diabetes are based on man-made medicines/ oral hypoglycaemic agents, which are effective, but have also been found to cause adverse effects and alter the metabolic and genetic pathways (Al-Alawi *et al.,* 2017). It is for this reason that the use of natural products (such as Ajwa dates) is a good approach to control diabetes, as they are less toxic and free from side effects. Miller *et al* (2003) conducted a study whereby they found that a diet including dates with yoghurt could have a beneficial effect on glycaemic and lipid control in diabetic patients. This study was conducted on healthy participants, hence the same batches of dates and yoghurt were used for all

participants. However, it wasn't allowable for diabetic patients to eat the same amount of dates as the healthy subjects, which was 6 to 8 dates. Although the exact mode of action of dates in the control of diabetes is not fully known, it has been suggested that it might be due to an increase in the output of insulin and inhibition of glucose absorption, which is an effect that plants have shown to have on managing the function of pancreatic tissues (Malviya *et al.,* 2010 and Fatima ,2012)

Ajwa dates, like other plants, plays an anti-diabetic role as they contain the active component of the PDE antioxidant. A recent study (Michael *et al.,* 2013) looked at flavonoid compounds from date fruits and showed that PDE plays an important role in the improvement of the different biochemical results in diabetic rats. Furthermore, Zhang *et al* (2015) claim that the strong antioxidant profile of the Ajwa fruit can play a strong anti-diabetic role by scavenging the free radicals. Moreover, Hussain Mallhi *et al* (2014) claim that the richness of flavonoids and phenols in Ajwa date extracts could be the reason for their anti-diabetic activity, which can play a role in controlling diabetes as the phenolic compounds also modulate the secretion of insulin in the human body. Hasan and Mohieldein (2016) also found that consuming Ajwa seed extract by water (100g/L) had a significant reduction in the blood glucose level of streptozotocin diabetic rats due to the control of oxidative stress. However, the small sample size of Hasan and Mohieldein's study were one of the limitations of their study. Their study (ibid, 2016) was an animal expiremintal study and this type of study is weak compared with the human trials. There is a further research is needed to test the hypothesis that Ajwa dates have good impact on blood glucose level on human.

2.10.5 Ajwa dates and blood pressure

The pressure of blood in the arteries fluctuates between heartbeats. It will be highest when the heart contracts and pumps blood throughout the body (Systolic Blood Pressure, SBP also known as the upper number), and lowest when the heart relaxes, while it fills with blood before pumping again (Diastolic Blood Pressure, DBP, also known as the lower number) (Amery *et al.,* 2012).

Hypertension can be defined as high blood pressure that causes a rise in the systolic blood pressure (SBP) and an increase in the level of diastolic blood pressure (DBP). The SBP is the upper number and a high level would have a

detrimental effect on human health (Lawes *et al.,* 2008).

The British Heart Foundation (BHF) reported that the normal and healthy level should be in the range (90/60 mmHg to 120/80 mmHg). Furthermore, Lawes *et al* (2008) highlight that patients with a high blood pressure (more than 140/90 mmHg) have damage in the wall of their arteries, which leads to a higher risk of heart attack or heart diseases (such as stroke, clot and CVD). Most patients with hypertension (high blood pressure) do not know that they have the disease, which is why hypertension is named the “silent killer” as its symptoms (headache, dizziness and in some cases visual disturbances) remain unnoticed for years before diagnosis (Amery *et al.,* 2012).

Ekmekcioglu *et al.,* 2016 reported that an increased dietary intake of potassium and decreased consumption of foods containing sodium, have a beneficial effect on hypertension patients. Ajwa dates contain important minerals such as potassium, which play a vital role in controlling high blood pressure (Assirey, 2015).

Summary

In summary, the Ajwa date has a rich source of antioxidants and the highest amount of polyphenols when compared to other types of dates. Data analysis from the last few decades suggests that Ajwa dates have a potential to become an essential food ingredient for developing new bioactive functional food products targeted at various physiological functions of the human body. In addition, the Ajwa date is eaten at the tamr stage, whereas the highest nutritional value is at the kimri stage, which is why most studies used Ajwa seed extract rather than the flesh of the Ajwa date. Although recent animal studies have provided evidence for the effectiveness of Ajwa dates, there is a need for quantitative studies on humans, to provide a better understanding of the protective actions of Ajwa dates and the exact mode of action of Ajwa dates in the control of diabetes.

Chapter 3 Methodology

3.1. Introduction

This chapter provides an overview of the research approach used for this study. Details of various factors such as, ethical considerations, the study design and duration, sample size and selection and methods of data collection will be explored. Thereafter, the validity and reliability of the study will be evaluated, followed by the statistical methods used and a justification of the choices made by the researcher to end the chapter.

3.2. Ethical considerations

Approval was given by the Manchester Metropolitan University (MMU) ethics committee on 2 April 2013, for the participation of (non-diabetic) volunteers as a healthy group. The research ethics committee of Al-Noor Specialist Hospital, Makkah, Kingdom of Saudi Arabia (KSA), granted official approval for the participation of patients with type 2 diabetes (Diabetic group) on 1 May 2015 (See appendix 11) and request for the approval was submitted to the ethics research committee at MMU and approved on 16th May 2013. Patients were informed of the aims of the study and recruited after providing written consent to participate.

3.3. Determination of sample size and study duration

3.3.1. Sample size for main study

Having considered the findings of studies in the field since 1997, it is evident that the sample size that showed significant validated results ranged between n= 16 to 159 (Bamosa *et al.*, 1997; Bamosa *et al.*, 2010; Shah *et al.*, 2012 and Fallah Hoseini *et al.*, 2013). These earlier studies noted that the sample size with the most improved change to control glucose profile and lipid profile ranged from n=60 to n=80 (Mohtashami and Entezari, 2016).

Therefore, at the beginning of this study, 180 subjects were recruited with the intention of providing at least 150 volunteers for the research; 75 participants for the trial 1 (diabetic) group and 75 volunteers for the trial 2 (healthy) group. As expected, from the 180 participants who initially joined the study and who fitted the eligibility criteria, some failed to complete the therapy regime, hence dropping out from the study and some of them were barred by specific exclusion criteria (patients unwilling to continue the trial). By the end of the study, 75 participants were randomly selected for the diabetic group and 75 participants were randomly selected for the healthy group. In total, 30 participants were

eliminated from the initial 180 volunteers, until the researcher had 150 participants altogether (75 participants for each trial).

As illustrated in figure 3.1, 15 patients failed to complete trial 1. There were various reasons for this including: n=7 failed to continue the study and n=8 of the diabetic patients were removed from the study. The details for those who left the study after recruitment at Al-Noor hospital are as follows: 3 failed to complete the study, due to 2 of them having cardiovascular disease (CVD) and one of them having lung cancer. The other diabetic participants (n=5) were eliminated because they missed FBG measurements. The other seven diabetic participants who were eliminated stopped taking part in the study.

From figure 3.2 below it can be seen that 15 participants were eliminated from trial 2: n=6 failed to complete the study due to missing measurements (FBG, 2hPP) and n=9 of the healthy subjects were excluded from analysis. All patients were given a supplier of Ajwa dates it is sufficient to finish in 12 week, two patients (n=2) were eliminated because they consumed all the Ajwa dates supplied for the 12 week study within 1 month of the start. For those were assigned to the *Nigella sativa* seeds, C-NS (n=6), the reasons for their failure to complete the trial was that participants travelled abroad (n=3) at week 6 of the study, and the others (n=3) ceasing to follow the diet and eating *NS*.

3.3.2. Study duration

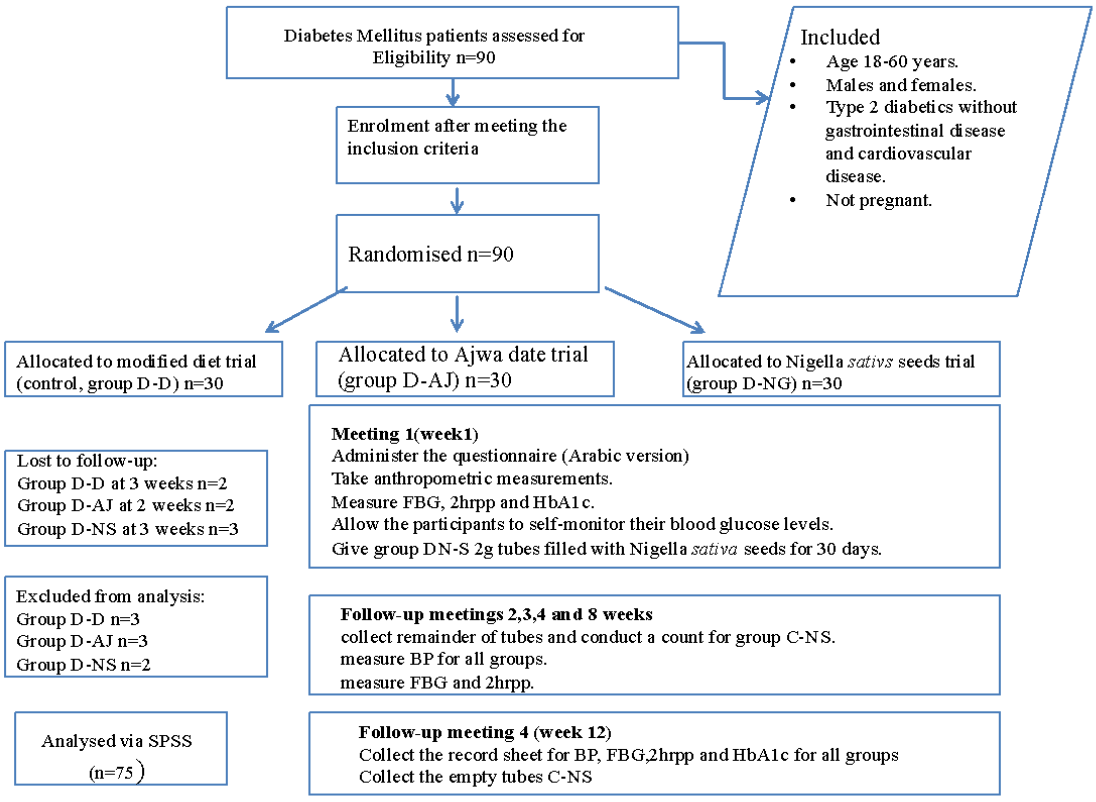
Initially, the choice of the study period was based on a previous study by Bamosa *et al*, (2010), which reported that there is a significant reduction in fasting blood glucose (FBG), two hours postprandial blood glucose (2hPP) and glycated haemoglobin (HbA1c) following 3 months of daily consumption of *Nigella sativa* seeds (2g/day). On the other hand, Datau *et al*, (2010) found that there was no significant decline in blood pressure and fasting blood glucose with a dose of 1g daily of *Nigella sativa* seeds. Although the study of Bamosa (1997) demonstrated that 2 weeks was sufficient to show a reduction in FBG after a daily consumption of *Nigella sativa* seeds, Kaatabi *et al,* (2015) suggested that a longer duration is needed to illustrate the beneficial effect of *Nigella sativa* seeds on glucose markers. Thus it was determined that a longer duration was needed to result in a beneficial outcome with regards to FBG, 2hPP and HbA1c levels (Najmi *et al.*, 2008 and Kaatabi, 2015). Therefore, based on the findings of the above mentioned studies, the researcher chose

the duration of this study to be to 90 days of treatment, with measurements being taken weekly.

3.4. Trial 1 (Diabetic Type 2 Group)

3.4.1. Study design and study population

Ninety Saudi male and female type 2 diabetes patients were recruited for the study from Al-Noor Specialist Hospital in Mecca, KSA, between July and October 2015. Participants who met the inclusion criteria (Figure 3.1), were randomly allocated to one of the following three test groups, ensuring equal numbers in each group: group 1 consumed a modified diet for 12 weeks (group D-D)., second group were given Ajwa date daily in conjunction with a modified diet for 12 weeks (group D-AJ). Third group consumed 2g of *Nigella sativa* seeds daily plus modified diet for 12 weeks (group D-NS).The timeframe (over a period of 12 weeks) and study outline are detailed in Figures 3.1



2hrpp: 2-hour postprandial glucose, BP: blood pressure, FBG: fasting blood glucose, HbA1c: haemoglobin A1c, SPSS: statistical package for the social sciences

Figure 3.1. Study design and progression flow chart for Diabetic group

3.4.2. Recruitment and selection of participants

Included in the diabetic group were patients with type two controlled and uncontrolled diabetes, either attending the outpatient diabetes clinic or admitted into Al-Noor Specialist Hospital. At the Al Noor hospital, the dietitian and the doctor who were responsible for the diabetic patients were with the researcher throughout the study to make sure that all the diabetic patients who took part were not placed under any risk (such as high blood glucose levels) by the modifcations the study required to their diets. The trial 1 participants (diabetic patients) were selected randomly using a randomised clinical trial (RCT).

During the selection stage of the diabetic participants in Makkah, the researcher checked through and reviewed the hospital files of 300 patients. Patients who fitted the inclusion criteria and were thus eligible to participate, were invited to take part in the study. The dietician at Al-Noor hospital had more than 20 appointments daily, which comprised of new patients and others on a follow up meeting. Most of the diabetic patients do regular test (BGL) before their appointment. Most patients brought this result with them to the meeting with the researcher, however some did not bring the result with them so the researcher asked the nurse for this data. This ensured that for all patient had an updated analysis result at the beginning of the research.

Participants were recruited by approaching diabetic patients at the dietician clinic in the hospital. Patients attending the clinic appointments were presented with an outline of the study and information as to the possible benefits of *Nigella sativa* seeds and Ajwa dates with respect to their ability to control blood glucose levels. The patients were randomly allocated to one of the three groups, depending on the order in which they attended their follow-up appointment with the dietician. The researcher allocated the first attending patient to group D-D, the next patient to group D-AJ, and the next to group D-NS, and so forth, until all of the participants had been allocated to a group.

The researcher explained the aim of the trial to the diabetic participants, in Arabic, and provided advice with regards to the dietary plan plus treatments with *Nigella sativa* seeds and Ajwa date respectively. Patients were fully informed about the purpose and duration of the study, and were reassured that they could leave the study at any time. The diabetic patients, who agreed to

participate in the study were asked to sign the Arabic version of the consent form (see appendix 13) and to read an information leaflet about the research and to fill out the questionnaire (demographic, lifestyle and diabetes sections) (See Appendix 12).

They were also asked to adhere to the instructions given in relation to the modified diet (see appendix 15). The modified diet comprised of five meals, with a choice of seven varieties for each meal from which the participants could choose (see appendix 14). Each participant was also provided with either *Nigella sativa* seeds tubes or Ajwa dates, depending on their allocated group, during a meeting which lasted approximately 25 minutes (See appendix 16).

All the diabetic participants were requested to perform self-monitoring of their blood glucose (SMBG) and to determine their FBG and 2hPP before the initiation of therapy, after Day 1 and Day 7, then weekly thereafter for 12 weeks. The SMBG readings were reliable up to 10 mg/dl (Schnell *et al.,* 2015). In addition, the researcher reviewed the participant's initial fasting blood glucose (FBG), two hours postprandial blood glucose (2hPP) and blood pressure (BP) measurements as well as their height and weight.

The anthropometric measurements (weight and height) and body mass index (BMI) were taken for each patient before the initiation of treatment and after 12 weeks. Measurements were carried out for the patients at baseline (Week 1), then subsequently at Weeks 4, 8 and 12 after starting the therapy. The measurements taken were blood pressure (BP), fasting blood glucose (FBG) and two hour postprandial blood glucose (2hPP).

The follow up stage was very important as it provided the researcher with the opportunity to measure blood glucose levels, blood pressure and anthropometric measurements, as well as replace the *Nigella sativa* tubes and collect the blood glucose level records. Follow-up meetings were scheduled at weeks 4, 8 and 12. The study participants were asked to record any changes with regard to their lifestyle or body weight, and instructed to inform the researcher if they consumed any other food not included in the modified diet designed by the researcher.

Group D-NS was assigned consumption of the modified diet, plus 2g of *Nigella sativa* seeds daily, for 12 weeks. This dose was chosen as an effective dose for

the maintenance of blood glucose levels, following the findings of a study by Bamosa *et al,* (2010), who used different *Nigella sativa* seed doses (1g, 2g and 3g), and found that a 2g/day dose was the most effective. These three doses were also used in other studies that looked at the effect of *Nigella sativa* seeds on patients with diabetes. Having considered the findings of previous research (e.g. Kaatabi *et al.,* 2015), for this study it was decided that a dose of 2g/day would be used.

At the end of the study, 75 participants with type 2 diabetes completed trial 1 and had a full set of results. To summarise:

- 25 participants consumed the modified diet for 12 weeks.
- 25 participants consumed the modified diet, plus 2g of *Nigella sativa* seeds daily, for 12 weeks.
- 25 participants consumed the modified diet, plus one Ajwa date every day, for 12 weeks.

3.4.3. Inclusion and Exclusion criteria

The following inclusion criteria were used to select the type 2 diabetes patients:

- Male and female Saudis with type 2 diabetes.
- Those with both poorly controlled and well controlled type 2 diabetes.
- Those aged 18–60 years.
- Residents of Mecca, to facilitate follow-up sessions.
- Those who agreed to sign a consent form.

Exclusion criteria for this study were as follows:

- Pregnant women.
- Those with type 1 diabetes.
- Patients with chronic renal disease.
- Patients with cardiovascular disease.
- Patients who had consumed *Nigella sativa* seeds or any other herbal treatment to control their diabetes in the last 12 weeks.

3.5. Trial 2 (Healthy Groups)

3.5.1. Study Design and study population

Initially, the healthy group for this study consisted of 90 healthy (i.e. non-diabetic) male and female participants recruited from Manchester student societies (MMU students, Asian/ Arab background) with the aim of registering 75 healthy subjects for the study. They were split into three equal groups of 30, the first group consumed a modified diet (C-D), the second group consumed the modified diet plus 2g of *Nigella sativa* seeds (C-NS) daily for 12 weeks, and the third group consumed the modified diet, plus one Ajwa date (C-AJ), daily, for 12 weeks. Figure 3.2 shows the process for allocating the healthy participants who met the inclusion criteria. All the healthy participants were from an Asian or Arab background and were used to consuming AJ and Ns. The healthy subjects were willing to participate because eating Ns and AJ was part of their cuisine and traditional habit.

Table 3.1. The study design for the clinical trial (SA)

Group	Study population	Age	Sample size (N)	Study duration
Controlled group (Non-diabetic)	In Manchester, UK, of Arab/Asian background	18 – 60 years	90	12 weeks

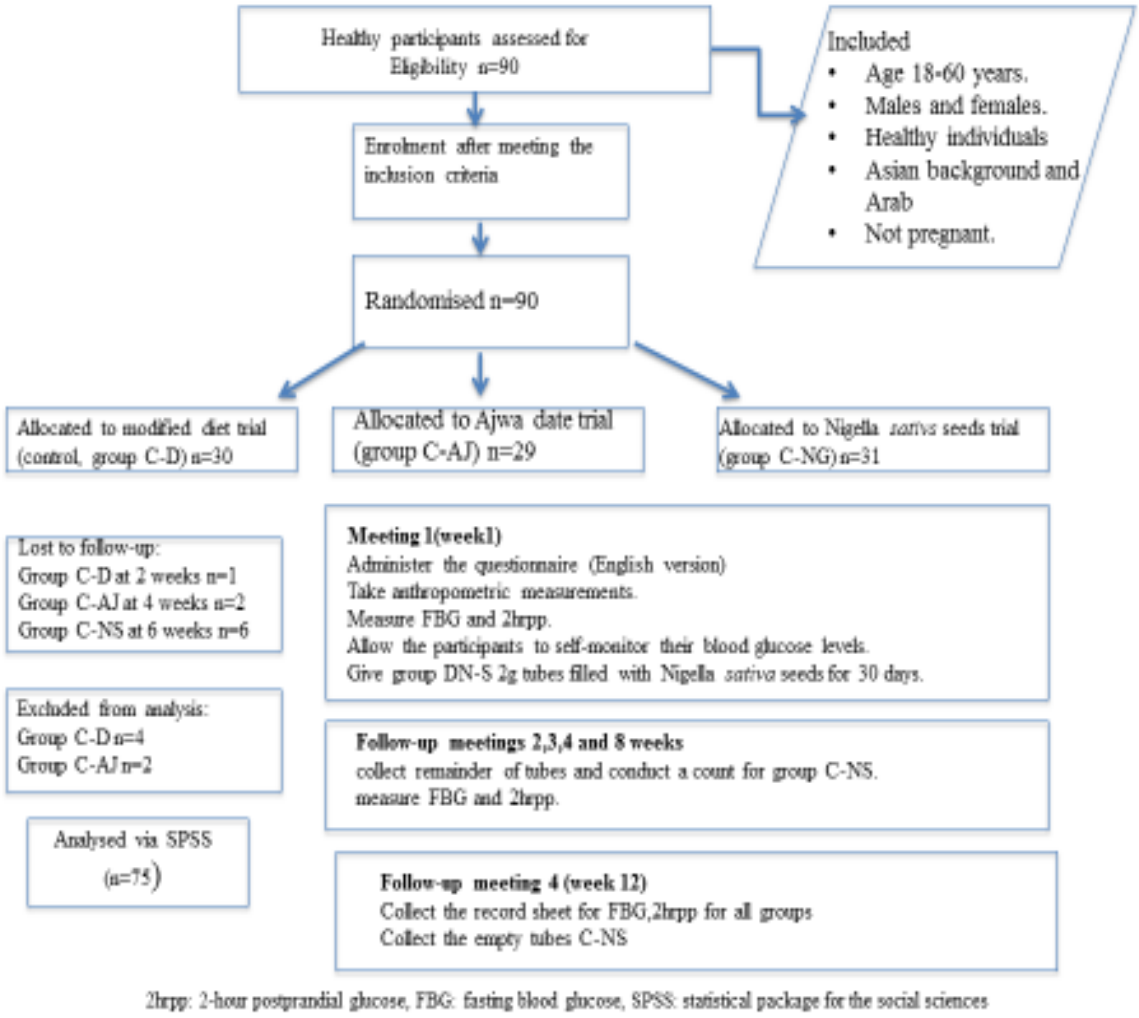


Figure 3.2. Study design and progression flow chart for healthy (non-diabetic) group

3.5.2. Recruitment and selection of participants

The non-diabetic (healthy) participant target population consisted of males and females originally of Asian descent (i.e. Gulf Arabs, Malaysian and subcontinental Asian (covers India, Pakistan and Bangladesh), aged 18–60 years and living in Manchester. The trial 2 (healthy group) was selected using a randomised clinical trial (RCT) and the participants from the UK study gave consent to take part and were recruited randomly from MMU. Everyone who took part was a willing volunteer and the study had been passed by the Ethics committee.

After initially recruiting 90 healthy participants, only 75 healthy male and female participants in the UK were actually included in the study, and were then split into three equal groups of 25 people. The first group consumed a modified diet (C-D), the second group consumed the modified diet plus 2g of *Nigella sativa*

seeds daily, for 12 weeks (C-NS), and the third group consumed the modified diet, plus one Ajwa date daily, also for 12 weeks (C-AJ).

Due to the study being carried out at Manchester Metropolitan University physiology lab, and having received permission from the university to distribute a booklet containing information on the study, the best place to recruit non-diabetic subjects, who were originally from an Asian or Arab background was the university's Islamic societies and the local mosques.

At the selection stage the researcher received calls and text messages from participants responding to adverts. The recruitment of participants for the study was achieved via flyers (see appendix 9 and10) and by sending emails through the university and by face to face interaction with students outside the university. After receiving positive responses from the participants stating that they were willing to join the trial, the researcher selected the healthy volunteers based on inclusion and exclusion criteria. Then the researcher invited the healthy subjects (via a telephone call or using Whatsapp) to visit the lab in order to take the initial measurements for weight, height and blood glucose levels. In order to take the preliminary measurements such as FBG (Fasting blood glucose), weight and height, the researcher made an appointment with the healthy subjects, and asked them to fill out the questionnaire (demographic section and lifestyle section) and sign the consent form (See Appendix 2 and 3). The participants were given the instructions of the study and a dietary plan to follow (See Appendix 4 and 8). Healthy participants were requested to follow a modified dietary plan and maintain normal physical activity throughout the trial. The subjects were provided dietary advice and instructions (See Appendix 4 and 5) in order to complete the trial in a good way. The participants who were in the Ajwa group, were asked to avoid eating other types of dates while participants in the other 2 groups (*Nigella sativa* and modified diet) were asked to avoid eating Ajwa dates. Each of the participants met the researcher for about 15 to 20 minutes, as documented in the time schedule (see Appendix 17)

The possible benefits of *Nigella sativa* seeds and Ajwa dates on health were explained to the participants at the first meeting (see appendix 1). They also received training from a technical officer on how to self-monitor and measure their blood glucose levels (details mentioned in section 3.6.6). After the

induction meeting, the researcher contacted the participants once a week to record their fasting blood glucose, FBG (before meal) and two hours postprandial blood glucose, 2hPP (after meal) measurements. Regular meetings, four meetings over 12 weeks, took place between the researcher and the participants to ensure compliance and to address any problems.

Participants were asked to perform SMBG (Self-Monitoring Blood Glucose) with respect to their FBG at home. The FBG and 2hPP results were collected by the researcher on a weekly basis. Physical activity was recorded daily to ensure that the data collected was valid and reliable.

3.5.3. Inclusion and Exclusion criteria for the healthy group

Selection criteria for the inclusion of non-diabetic or healthy subjects in the study were as follows:

- Males and females from an Asian background, for example, Arab, Indian, Pakistan, Malaysian and Bangladeshi, also must be living in the UK.
- Those aged 18–60 years.
- Those who signed a consent form.
- Those living in Manchester to facilitate follow-up sessions.
- Non-pregnant women.
- Healthy participants.
- Participants had to agree to follow the diet and perform the measurements at home weekly (FBG and 2Hr-PP)

Exclusion criteria:

- Participants with T2DM, CVD or BP patients.
- Participants with regular consumption of any type of dates.
- Pregnant women.

3.6. Data collection and processing

3.6.1. Questionnaire design for trial 1 and 2

Initially, the researcher checked that the volunteers met the inclusion criteria and that they were happy to participate in the trial, and then they completed the questionnaire (Arabic version for intervention group and English version for controlled group). Regarding the diabetic patients, the questionnaire was read out for those who struggled to read.

The questionnaire was designed to collect information from the volunteers and was divided into three sections: the first section was intended to gather personal background information, the second section gathered lifestyle data and the third section was only applicable to diabetics in order to collect medical health data. In addition, the questionnaire was designed with simple words written in English and then translated into Arabic. The participants were asked to complete a short questionnaire providing demographic information such as name, age, gender, marital status, smoking habits, diabetes status, age at diabetes onset, medical history and BMI. The designed questionnaire was pre-tested on 25 Arab volunteers who lived in the UK to identify apparent errors and was corrected to improve the clarity of instructions and remove irrelevant and unclear questions. “Informed consent” can be defined as the study participants agreeing to take part therein, based on the provision of clear information and their ability to easily understand it (Franck and Winter, 2004). Thus, the information in the consent sheet was explained to the participants, who confirmed that they understood the study procedure and requirements, then agreed to participate in the trial. In addition, details of the study, what the treatment involved, the benefits and potential side effects were outlined to the study subjects. Study subjects needed to be familiar with the purpose of the study, its possible benefits and whether or not it could be harmful. It is critical that simple language that is easy to understand was used in the consent form. The consent form and information sheet for this study were written in English and then translated into Arabic.

3.6.2. Dietary design for Trial 1 and 2

Table 3.2. The DASH diet plan for 2000 calories a day for health conditions (High blood pressure patients) (NIH, 2003)

Food group	Daily Serving	Serving size
Wholegrain	7-8	1 cup ready to eat cereal ½ cup cooked rice
Vegetables	4-5	1 cup raw leafy vegetables
Fruit	4-5	1 medium fruit ¼ cup dried fruit
Low fat or fat free dairy food	2-3	1 cup yogurt
Lean meat and poultry	2 or less	3 ounce cooked lean meat (skinless)
Nuts and seeds	4-5 per week	½ cup cooked dry beans 1 teaspoon soft margarine
Sweets	5 per week	1 tablespoon sugar
Fats and oils	2-3	1 teaspoon vegetable oil

The modified diet was designed by the researcher using the diabetes pyramid and the Dietary Approaches to Stop Hypertension (DASH) plan, which highlights the importance of sensible food selection. Figure 3.3 below details the formation of the food pyramid. The base group shows that eight to ten servings of starchy food should be eaten for every three to four servings of vegetables and two to four servings of fruit. As the dairy group contains high amounts of carbohydrate, which may affect blood glucose levels, two servings of dairy products should be consumed. The final group suggests a daily consumption of four to seven ounces of meat (NIDDK, 2007). The diabetes food pyramid in Figure 3.3 is designed for diabetics to choose food proportions easily. The food group at the base of the pyramid contains grains, starchy foods, vegetables and beans. More can be eaten from this group compared to the fats and sugars group at the top of the pyramid (NIDDK, 2014).

This diet is designed to control and monitor the blood pressure in the body. This diet plan is outlined in the Table 3.2 and is based on the intake of wholegrain, poultry, reduced amounts of fat, sugar and salt. In addition, this eating plan has rich sources of minerals such as potassium, magnesium and calcium. Diabetic patients are encouraged in their diet plan to have whole grains, fruit, vegetables, legumes and other rich sources of carbohydrates. However, it is essential to manage and count carbohydrate servings per day to ensure not too much gets consumed (Sacks *et al*., 2001; Liese et al, 2009).

The modified diet created for the participants, is based on an average calorie intake of 1900 - 2000, also taking size, weight and exercise into consideration. As a whole, daily calorie consumption should total between 1900 to 2000 calories for females and 2000 to 2500 calories daily for males. The UK government recommend that a daily calorie intake of 1900 to 2500 is suitable for men who do not undertake regular physical activity (NIDDK, 2007; DRVs, 2011). As a result, the modified diet designed for the participants totalled 1600 to 1800 calories; an additional 600 calories was made available for those volunteers who felt hungry or exercised daily. The modified diet was designed for both healthy and diabetic participants, so the food choices were a part of their traditional cuisine. All the male participants were verbally told that they were allowed some choices of certain snacks of an additional 600 calories per day if they were hungry. The rationale for the additional 600 calories designed for the male participants, who had 1700-1800 calories was that it was the midpoint of the recommended requirement needed per day (male 2000 to 2400 calories). By adding an additional 600 calories, it allowed them to stay within the recommended daily consumption of calories, in order for the snack choices to be healthy. As for the female participants, they were told to only follow the modified diet of 1800 calories per day.

The recommendation and dietary guidelines for diabetes patients state that carbohydrates should provide 45% to 65% of total energy in their diet. Fats should provide 25% to 35% of total energy and protein should provide 12% to 20% of total energy (Geissler and Powers, 2005). Moreover, the modified diet was analysed by the WISP V3.0 intake analysis system to determine the percentages of macronutrients and micronutrients, and to ascertain the suitability of the modified diet. The analysis confirmed that the modified diet

would provide 50% of required energy from carbohydrates, 20% from protein and 30% from fats.

Table3.3. Mean intake for the modified diet compared with the Guideline Daily Amounts (GDAs)

Nutrient	Mean daily intake	GDA	% of GDA
Energy (kcal)	1600-1800	2000	76%
Protein (g)	50.0	50.0	100%
Carbohydrate (g)	205.0	260.0	79%
Sugars (g)	83.0	90.0	92%
Fat (g)	57.9	70.0	83%
Saturates (g)	18.8	20.0	94%
Fibre (g)	20.3	24.0	85%
Sodium (mg)	1995	2400	83%
Salt (g)	5.0	6	83%

Table 3.3 shows a comparison of the modified diet and the GDAs, indicating that the modified diet provides slightly smaller amounts of some components but is sufficient for good nutrition.

Figure 3.3. The Diabetes Food Pyramid (NIDDK, 2007)

The diabetes food pyramid above indicates that the best sources of starch are bread, cereal, crackers, lentils, rice, pasta, potato and corn. The modified diet contains whole grain starch, which is considered to be beneficial for diabetic patients. It also contains an appropriate balance of carbohydrate, vitamins, fibre and minerals (NIDDK, 2007). Vegetables were also included in the modified diet, as this group contains multiple vitamins, minerals and fibre. Vegetables such as celery, tomatoes, carrots, lettuce and broccoli are also a good source of carbohydrates. A selection of fruits was included in the modified diet, because as with vegetables, they also contain a vast array of vitamins, minerals, carbohydrates and fibre (NIDDK, 2014).

The modified diet included apples, berries, orange, strawberries, bananas and fresh fruit juice. The dairy category provided a rich source of calcium, protein, carbohydrate, vitamins and minerals – the only caveat being that milk had to be low fat skimmed. The modified diet also included items from the top of the food pyramid: meat, eggs, salmon, fish, peanut butter, tuna, lamb, low fat cheese and chicken - all foods high in protein. Products from this group should be consumed in smaller quantities than foods from other groups (NIDDK, 2007). When consuming foods from this group, it is essential to pick the healthiest means of cooking meat and poultry; for example by grilling, steaming and stir-frying, in order to significantly reduce the risk of cardiovascular disease in people with diabetes (NICE, 2014). British Nutrition Foundation (2016) reported that reheating cold starchy food such as potato, pasta, rice and bread could have an improvement in controlling BGL by reducing blood glucose.

Table 3.4. The serving size daily from the Diabetes food pyramid (NIDDK, 2007)

Food groups	Serving daily	Portion size
Starches	6-11	1/3 cup cooked rice, ½ cup pasta , ½ cup beans
Vegetables	3-5	1 cup of raw vegetables, ½ cup cooked vegetables
Fruits	2-4	1 medium fresh fruit, ½ cup fresh fruit, ¼ cup dried fruit
Meat and meat substitutes	2-3	2 eggs, 2oz of fish, meat, 4tbsp peanuts butter
Milk and dairy product	2-3	1 cup of low fat milk, ¾ cup plain yogurt
Fat and sweet	0-3	Butter, oil, 1 tbsp salad dressing, 6 nuts

The Dietary Reference Values (DRVs) for nutrient intake recommend that, for the nutritional management of diabetes, the amount of fats (particularly saturated fats) in the diet should be limited. An accepted figure is that saturated fats should be equal to or less than 10% of total energy consumed (NIDDK, 2014). Alongside this, cholesterol intake should be reduced to less than 300mg per day. Nutritional management assists in controlling blood glucose levels

hence reducing the risk factors associated with diabetes. (Geissler and Powers, 2005). As a result, Geissler and Powers (2005) also state that the limiting of fats can help diabetic patients to control blood glucose levels because fats within the blood can block insulin from reaching the blood cells.

3.6.2.1. Nutritional Analysis for Modified Diet

Analyses of nutrition and food groups for the modified diet were conducted using NetWisp V3.0 (a product by Tinuveil Software), a dietary analysis software program that analyses and converts dietary intake measures and converts them into energy, macronutrients and micronutrients. All food composition data is supplied from HMSO/OPSI, McCance and Widdowson's Food Composition Table, 5th and 6th editions and supplements. (Hassan, 2015 and Murray et al, 2013)

NetWISP V3.0 includes data from the following : Tillery Valley Foods (2008) ,Calypso Soft Drinks Ltd (2008), Brakes Food Service (catering) products (2008), Nutricia (tube and sip feeds, 2008), Abbott (tube and sip feeds, 2006), Glycaemic Index of Foods (2005), Better Hospital Food (2005), Pasta and Pasta Sauces, Food Standards Agency (FSA) (2004), Catch-Up Project, FSA (2004), AOAC Fibre Content of Foods, USDA (2004), Non-milk Extrinsic Sugar Content of Foods, calculated by Registered Nutritionist (2003) (Murray *et al.,* 2013).

Nutrients for the modified diet were analysed. Energy in calories and macronutrients, such as carbohydrates, proteins and fat (total fat, cholesterol, saturated fatty acids, monosaturated and polysaturated fat) were also analysed. Micronutrients analysed included vitamins C, B12, D, A and B6, niacin, riboflavin, thiamin and carotene. Other nutrients analysed included sugar, non-milk extrinsic, starch, fibre, chloride, selenium, sodium, potassium, phosphorous, magnesium, calcium, iron, copper, zinc and manganese (Murray *et al.,* 2013; Institute of Medicine, 2011).The daily calorie consumption of a healthy adult should roughly be 2000 for women and 2500 for men (DRVs, 2011). However, in Saudi Arabia the daily energy intake is between 1870 and 2290 calories (Hamad, 2015).

3.6.3. *Nigella sativa* seeds preparation

Nigella sativa seeds were given to the participants who were advised to consume 2g doses daily for 12 weeks. The *Nigella sativa* seeds, produced in India. The NS seeds were ordered once to ensure that the Ns were from the same batch (from Just Ingredients products company) to be used for both trials 1 (diabetic patients) and 2 (healthy participants). It was ordered online by MMU staff and prepared in 2g aliquots to provide sufficient amounts for all participants in the NS groups for the entire duration of the trial. The *Nigella seeds* were weighed using a Mettler® PL3000 silicone weighing bowl, then each aliquot was placed in a small tube at the human physiology studio at MMU, as shown in Figure 3.4.It was advised that all participants chew the *Nigella sativa* seeds and not swallow them whole. For consistently it was requested for all participants should take *Nigella seeds* in the morning and record the time.

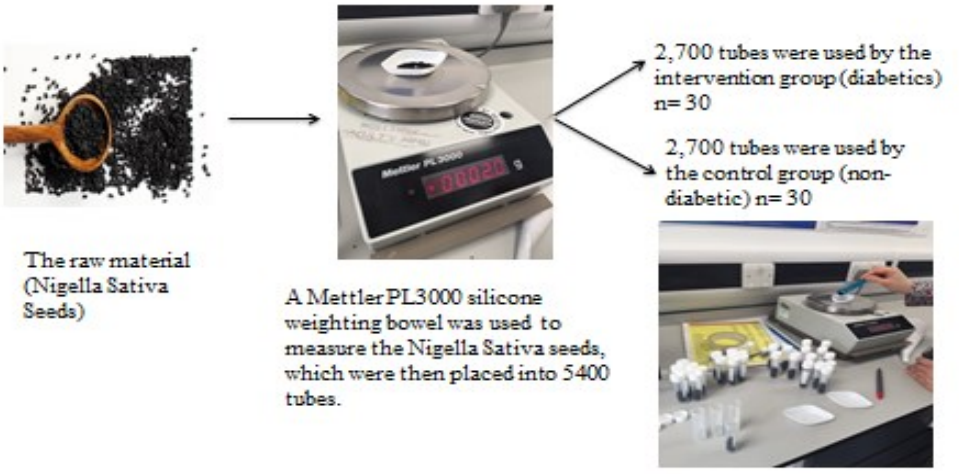


Figure 3.4. A flow chart demonstrating the process followed when measuring out the *Nigella sativa* seed doses

3.6.4. Ajwa dates preparation

Ajwa dates, which are only grown in the city of AL-Madina, KSA, were provided to the relevant participants. The Ajwa dates were ordered online by MMU staff in one go, and the suppliers (Al-Madina Al-Menawara) were kept the same for T1 and T2 to ensure that the dates were from the same batch so that the Ajwa were from the same source.

The participants agreed to consume one Ajwa date in addition to a prescribed diet daily for 12 weeks to determine whether or not there was a beneficial effect on their blood glucose levels. Each participant was provided with a box of AJ dates containing enough dates (800g) and the researcher carefully explained that they should eat 1 AJ each day. At the end of each meeting (assessment meeting), they were asked them how many dates they had eaten and count the stones and collect them. Doing this allowed the researcher to identify the participants who did not follow the rules or the instructions given, and who had eaten all the AJ dates. For those who did not follow the guidelines provided, they were excluded.

The nutritional information as displayed on the box, is shown below in Table 3.5 and it appears from that this type of date is rich in fibre and carbohydrates.

Table 3.5. The nutritional facts for Ajwa dates (serving size 100 grams)

Nutrition information	Amount per serving	% Daily Value
Calories	282	
Calories from fat	3	
Total fat **Saturated fat** **Trans fat**	0g	0%
Cholesterol	0mg	0%
Sodium	2mg	0%
Total Carbohydrate	75g	25%
Dietary Fibre	8g	32%
Sugar	63g	
Protein	2g	
Vitamin C		1%
Iron		6%
Calcium		4%

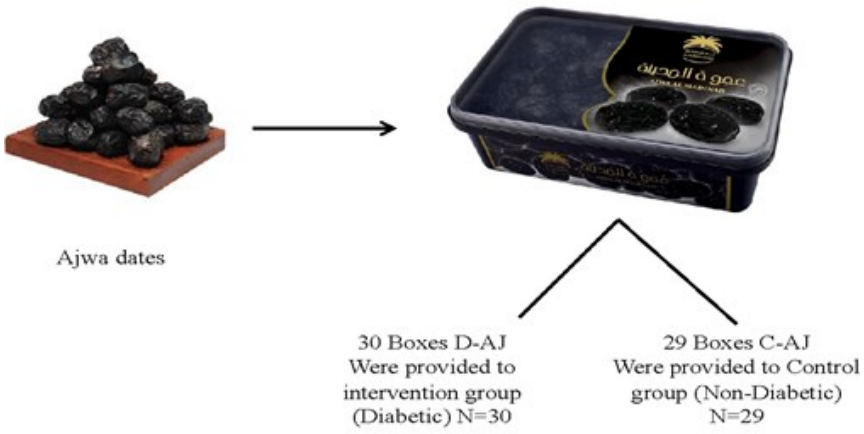


Figure 3.5. A flow chart showing the process for Ajwa dates

As shown in figure 3.5 above, it was provided 1 box of Ajwa dates for each participants and each box contains 91 Ajwa dates (800 g) during 12 week. Ajwa dates labels shows that dates has rich in source of minerals such as calcium, manganese, copper, magnesium, iron, potassium and phosphorus. Also have volatile oils, rich in fibers, vitamin B6, folic acid, proteins and sugar. The researcher asked the participants to keep the stones for Ajwa dates.

3.6.5. Anthropometric measurements for Trial 1 and 2

Weight and height were measured by the researcher at baseline and then at week 12. Participants were asked to stand barefoot and upright, with their backs against the wall and a free-standing stadiometer was used to measure their height (WHO, 2013). Weight was measured using a standard weighing scale on a firm, level surface. Subjects had to wear light clothing and no shoes. After calibrating the scale, the weights of all subjects were recorded. This was completed before subjects had breakfast and weights were rounded to the nearest 0.1 kg. (CDC, 2009).

BMI is a parameter used to measure body fat and define obesity. It is calculated as body weight (in kg) divided by the square of the height in metres (m^2). The BMI classification ranges of normal weight is 18.5–24.9 kg/m^2, overweight 25.0–29.9 kg/m^2 and obesity ≥ 30 kg/m^2. BMI is directly related to glucose intolerance in diabetes. (Ganong, 2005; Mann and Truswell, 2007). BMI was used in this study because it has been proven to be a valid measurement of nutritional status, which has a strong relation with adiposity and leads to a high risk of diabetes (Narayan et al, 2007).

3.6.6. Blood glucose levels measurements (Trial 1and 2)

Self-monitoring blood glucose (SMBG) should be a routine for diabetic patients in order to check the blood sugar level. Participants should also take FBG and 2hPP readings twice a week. The expected target for blood glucose levels before consuming a meal should be between 70–120mg/dl (3.9 to 6.7 mmol/L) ; an ideal level of glucose two hours after eating a meal should be less than 180mg/dl(10.4 mmol/L). This monitoring can highlight aspects of hypoglycaemia (low blood sugar) and hyperglycaemia (high blood sugar) (Geissler and Powers, 2005 and IDF, 2009).

Home SMBG devices provide quick results accurately and can play an important role in controlling blood glucose levels (Guerci *et al.,* 2003). Self-monitoring is undertaken by pricking the side of the finger, using a sanitised lancet and then placing a drop of blood on a test strip. The control group tested blood glucose levels once a week, whilst the intervention group undertook the test twice a week; and both recorded the results on a specially designed form (IDF, 2009).

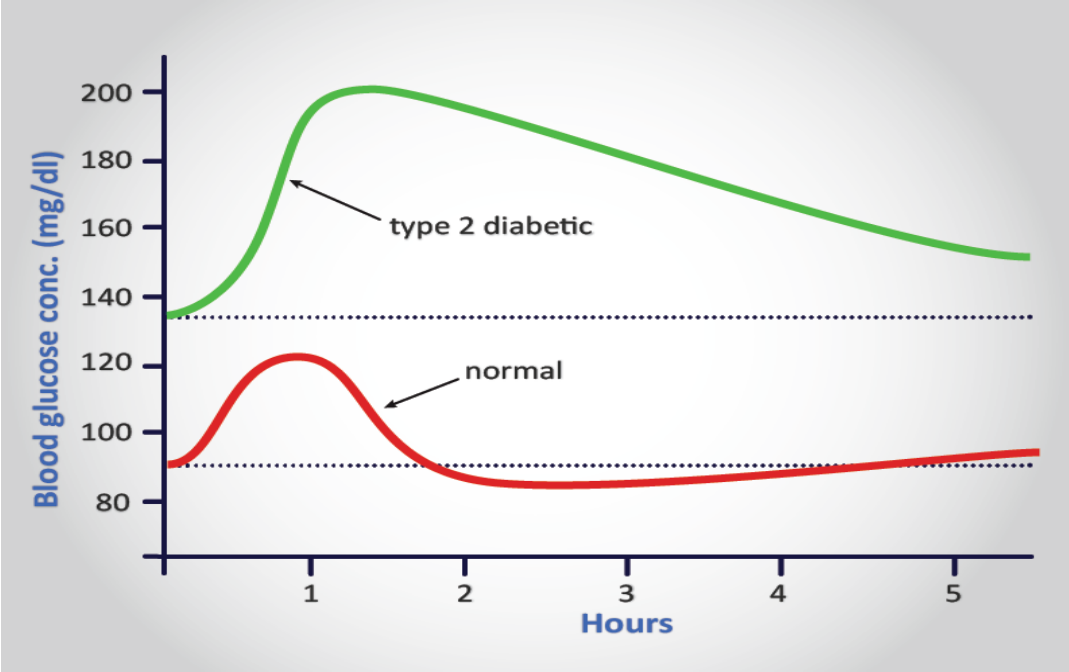


Figure 3.6. The blood glucose concentration in type 2 diabetes and normal people over time (King, 2013)

The line graph (3.6) above compares the concentration of blood glucose among type-2 diabetics and people who do not suffer from diabetes. The red line highlights a significant increase in blood glucose concentration in healthy people immediately after eating, peaking at 120mg/dl (6.7 mmol/L). After one

hour, there is a considerable decrease in blood glucose levels; after two hours, the concentration of blood glucose is relatively stable - below 100mg/dl (5.6 mmol/L).

Conversely, for patients with type 2 diabetes, the graph shows a rapid rise in blood glucose levels, peaking at 200mg/dl (11.1 mmol/L). an hour after eating a meal and remaining high for around four hours, with blood glucose concentration slowly reducing until it stabilises (Geissler and Powers, 2005). The lowest level for diabetics is less than the highest level reached by the healthy participants. Both sets of data increase by 30% but the diabetics' level does not fall back to the initial level, even after 5 hours. The blood glucose levels (FBG and 2hPP) of all participants were measured by the participants and they were recorded on the measurement sheet. In addition, the volunteers were asked to record the length of daily activity in the recording sheet.

3.6.6.1 Blood glucose measurements (monitoring systems)

Fasting blood glucose and 2 hours postprandial blood glucose levels were measured using the SD Codefree ™ blood glucose monitoring system. This kit included the SD Codefree meter, blood glucose test strips, check strip, a 3V battery, self-test diary, test strip package insert, carrying case, user instruction guide, lancing device and lancets. Subjects are supposed to be familiar with the instructions of the SD Codefree ™ blood glucose system.

SD Codefree blood glucose test strips include an electrode which measures the glucose level. The glucose level is determined in the blood plasma, which is mixed with the reagent on the test strip. The chemical reaction produces a small electric current. The SD Codefree meter measures the current and the result is displayed on the meter in mg of glucose per dl (mg/dl). It is very important for participants to wash their hands with warm water in order to increase the flow of blood, then to dry the hands (SD Codefree guide).

3.6.7. Glycated Haemoglobin A1c Measurement HbA1c (Trial 1)

HbA1c is a measure of the blood glucose level in diabetic patients over a three-month period. The HbA1c test, conducted by either a doctor or nurse, measured HbA1c using a DCA® Vantage Analyzer (made by Siemens), which indicates accurate results for diabetes and prediabetes. It is a simple four-step process where a finger prick blood sample is used and there is no need for patient

fasting. The same test kit is used for the diagnosis and management of diabetic patients. In addition, the results are available within six minutes.

For this study, the doctor or nurse at the diabetes centre at Al-Noor Specialist Hospital obtained a whole blood sample from the patients by performing a finger prick, from which the small drops of blood were captured in a 1µl capillary holder. The capillary holder was then inserted into the HbA1c reagent cartridge compartment. Thereafter, the reagent cartridge was taken to the DCA® Vantage Analyzer, and the barcode on the cartridge scanned. Following adherence to the on-screen instructions, the cartridge compartment door was opened, and the reagent cartridge inserted into the cartridge compartment, then the door was closed. The results were displayed on the screen six minutes later and printed out.The DCA® Vantage Analyzer determines the HbA1c level in type 2 diabetes patients.

Regular HbA1c testing is crucial for the optimum management of diabetes. Patients with type 2 diabetes need to control their blood glucose level, and this is achieved by maintaining a low-level HbA1c (the target/ideal is ≥ 6%). This decreases or prevents the development of complications associated with diabetes, such as foot, eye and kidney problems, not to mention cardiovascular disease (WHO, 2011).

Table 3.6. HbA1c Classification (WHO, 2011)

Haemoglobin A1c	**Interpretation of the result**
≥ 108 mmol/mol (12%)	Very high
86–108 mmol/mol (10–12%)	High
64–86 mmol/mol (8–10%)	A little high
≤ 53 mmol/mol (7%) (the target)	Ideal, maintain this level

3.6.7.1. The Test Principle for HbA1c

The intensity of the light transmitted through the cartridge optical window is analysed by the DCA Vantage Analyzer™ by using a spectrophotometer. Whole blood is added to the reagent cartridge, the cartridge is inserted into the DCA Vantage™ Analyzer, and then it takes 6 minutes to get meaningful results (see figure 3.7). The DCA Analyzer ™ performs all measurements and calculations automatically. The screen displays HbA1c percentage at the end of the assay. Inside the cartridge, the following chemical reaction takes place.

Measurement of total haemoglobin. To measure total haemoglobin potassium ferricyanide is used to oxidise haemoglobin in the sample to methaemoglobin. The methaemoglobin then mixed with thiocyanate to form thiocyanmethaemoglobin, the coloured species that is measured. The extent of colour development at 531nm is proportional to the concentration of total haemoglobin in the sample. Results are obtained by comparing the absorbance with results on a standard curve.

Figure 3.7. DCA Vantage Analyzer™ (Guide, 2008)

3.6.8.Blood pressure measurements (Trial 1)

The BP of the subjects was taken by the nurse while they were in a seated position, using an Omron® HEM-7113 Automatic Blood Pressure Monitor. BP was measured for the diabetic subjects at the beginning of the study, and every two weeks thereafter until completion of the study at 12 weeks.

Table 3.7. The classification of blood pressure (Lima *et al.*, 2015)

Blood pressure	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
Normal	≤ 120	≤ 80
Prehypertension	120–139	80–89
Stage 1 hypertension	140–159	90–99
Stage 2 hypertension	≥ 160	≥ 100

3.6.8.1. Blood pressure mechanism (oscillatory blood pressure monitoring principle)

Oscillatory devices present digital readings and operate on the principle that the flow of blood through an artery between systolic and diastolic pressure produces vibration in the arterial wall, which can be detected and transformed into electrical signals (Landgraf *et al.,* 2010). This oscillometric technique has been used successfully in ambulatory blood pressure monitors and home monitors. The way oscillometric devices operate, such as the Omron, is that a cuff has to be inflated over the upper arm. At full inflation of the cuff, there would be no blood flowing through the artery. By contrast, when the cuff is deflated below the systolic pressure and the pressure on the artery is reduced, blood is allowed to flow. This sets up a vibration in the wall of the artery which is detectable (Appel *et al.,* 2010).

After the cuff pressure drops below the patient's diastolic pressure, blood flows through the artery smoothly in regular pulses and without vibrations in the wall of the artery. Vibration occurs only where the pressure of the cuff is high enough for the blood to push the wall of the artery open so that it can flow through the artery. Vibrations are transferred from the wall of the artery into the transducer in the monitor through the air in the cuff. The transducer converts the measurements into electric signals. Oscillometric devices deflate at about 4mmHg per second. This renders them slower sometimes than auscultatory aneroid devices but they are known to be more accurate (Landgraf *et al.,* 2010; Ogedegbe and Pickering, 2010).

3.7. Validity and reliability

Validity and reliability are the two measurements of quality in a quantitative study. 'Validity' is defined as the strength of the final result. Ensuring the validity and reliability of the data collected is important in quantitative research (Golafshani, 2003).

The participants' personal information was treated as confidential and was not disclosed beyond the research team. The researcher ensured that confidential information was kept secure. All the results were entered into Microsoft® Excel® and doubled-checked to reduce mistakes or data entry errors.

To ensure validity and reliability in this study, patients in group D-NS (diabetics consuming *Nigella sativa* seeds) were seen at the dietician clinic once a month. Compliance, in terms of the correct amount of *Nigella sativa* seeds to be consumed daily, was ensured through a tube count, while the empty tubes were replaced on a monthly basis with new tubes. The healthy control group participants were seen at MMU once a month, where their empty tubes were also replaced with new tubes filled with *Nigella sativa* seeds (Zheng *et al.,* 2014).

Subjects in group D-AJ (diabetics consuming Ajwa dates) and group C-AJ (healthy controls consuming Ajwa dates) were seen monthly, for 12 weeks. Ajwa date stone counting was performed by collecting the date stones from the participants (n = 50). In addition, the researcher contacted the study subjects weekly by SMS, "Whatsapp|" messaging or by telephone call to remind them to measure their blood glucose (FBG and 2Hr-PP) and ensure that they were consuming the *Nigella sativa* seeds or Ajwa dates accordingly.

3.8. Compliance with appointments, measuring and diet

All the participants (the intervention group in KSA and the control group in UK) adhered to the measurements (self monitoring blood glucose SMBG) and followed the modified diet. Nuti *et al,* (2015) suggests that, all volunteers should have regular measurements consistently every week (FBG, 2hBG and BP) and regular communication by phone with the researcher in order to increase adherence.Therefore, participants had regular meetings with the researcher and medical staff. Those participants who did not adhere to the instructions of the study were excluded from the trial.

To make sure that literate patients understood the purpose of the study, the researcher emphasised the instructions and potential beneficial effects of *Nigella Sativa* seeds, Ajwa date and modified diet for the patients. The researcher encouraged the participants to record the measurements in the sheet (see appendix 7) to help the patients to remember to measure their SMBG at home. Participants from the Ajwa and *Nigella sativa* groups were provided with a chart to help them organise their measurement times weekly (measurements box) and remind them to take their *Nigella sativa* seeds doses on time (Graham *et al.,* 2016). It can help the patients to understand the purpose of the research if the instructions are reduced to several points and simple everyday language is used during each meeting, to ensure that they follow the diet recommendations clearly.

Regarding the adherence to measurements (SMBG), regular communication with patients and participants was maintained with the researcher by sending reminders to their phone via Whatsapp or SMS to help them to remember to take measurements. It has been reported that regular contact can significantly and positively impact on adherence to the research study. In this study tubes counting for *Nigella sativa* seeds, counting Ajwa dates seeds, checking the measurements weekly and regular assessment of participant activity leads to good adherence (Atreja *et al.,* 2005; Desroches *et al.,* 2011; Gaffari *et al.,* 2014 and Graham *et al.,* 2016).

The initial treatment for patients with type 2 diabetes is to follow a healthy diet plan combined with achieving control of the blood glucose level by doing SMBG at home and undertaking regular physical activity. So, an increased adherence

to lifestyle changes and dietary plan can control and even prevent further complications associated with diabetes.

For the patients, the new dietary plan and lifestyle changes can be very difficult for them to follow so they have difficulty in staying motivated and understanding fully the benefits in terms of the various food groups and having nutritional knowledge. For this reason, all the subjects were asked to report or note any changes in their diet during the research to enhance their adherence to this regime (See appendix 10) (Atreja *et al.,* 2005; Zweben *et al.,* 2009).

The modified diet was designed as a menu, where each meal in the menu had numerous choices. The participants could choose one option from each meal. They could consider how their choice complied with the dietary plan as a menu and they were given a variety of choices every day. (See appendix 15) Also, the dietary plan was designed using Saudi cultural routines in terms of eating patterns so, the participants were compliant with the plan and they accepted it because it conformed to Saudi cultural habits (Desroches et al, 2011; Gaffari et al, 2014).

3.9. Statistical analysis

A randomised controlled trial was conducted, meaning the patients who have a particular condition (intervention) were compared to healthy participants who did not have that condition. The primary aim of the research was to investigate the effects of consuming Ajwa dates and *Nigella sativa* seeds on the following clinical measures: Fasting Blood Glucose, Two Hour Postprandial Blood Glucose, Blood Pressure, and Haemoglobin A1c.

A statistical analysis was conducted to examine the effects of the consumption of three diets (the independent variables) on the repeated measures of five clinical observations (the dependent variables): Fasting Blood Glucose (FBG), Two Hour Postprandial Glucose (2HPP), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Haemoglobin A1c (HbA1c). Two trials were conducted. Trial 1 had 75 participants with Type II diabetes (termed the diabetic patients). Trial 2 had 75 participants who were not diabetics (termed the healthy participants). The two trials were conducted over a time period of 12 weeks. Four repeated measures of each dependent variable were collected on Week 1 (baseline), Week 4, Week 8, and Week 12 (endpoint).

Table 3.8 defines how the 75 diabetic patients and the 75 healthy participants were assigned into six equal sized groups, with 25 participants in each group. The three groups of diabetic patients were coded D-D, D-AJ, or D-NS. The three groups of healthy participants were coded C-D, C-AJ, or C-NS. The codes D, AJ, and NS indicated if the participants consumed a modified diet (D), a modified diet with Ajwa date (AJ), or a modified diet with seeds of *Nigella sativa* (NS).

Table 3.8. Groups of Participants

Trial	Group	Prescribed diet	Number of participants
1	D-D	Modified diet	25
1	D-AJ	Modified with Ajwa Date	25
1	D-NS	Modified with Nigella seeds	25
2	C-D	Modified diet	25
2	C-AJ	Modified with Ajwa Date	25
2	C-NS	Modified with *Nigella sativa* seeds	25

The randomized controlled trial (RCT) is the gold standard research design underpinned by the concept of evidence based practice (Satake, 2015). An RCT is designed to determine if a prescribed treatment has a statistically and clinically significant effect on participants who have been randomly assigned into two or more mutually exclusive groups. These groups include the intervention/treatment groups, who are exposed to the prescribed interventions/treatments, and the control groups, who are not so exposed.

Trials 1 and 2 were RCTs because the participants were randomly assigned into groups according to whether or not they received the prescribed diets. In experimental design terms, the healthy participants were a reference group, defined as a group of participants against which another group of participants (i.e. the diabetic patients) could be compared (Machin and Campbell, 2005).

The characteristics of the diabetic patients and the healthy participants were summarised using descriptive statistics. The values of the mean (M) and the standard deviation (SD) were computed for three continuous variables: age, duration of diabetes, and Body Mass Index (BMI). One ways analysis of variance was conducted to determine if these variables were different across the D, AJ, and NS groups. Frequencies were computed for the four categorical variables: sex, marital status, smoking, and education. Chi Square tests were conducted to determine if the frequencies were different across the groups of participants. Differences were by $p < .05$ for the test statistics.

The demographic and physical characteristics of the six groups of participants at the start of the study were summarized using frequencies for the categorical variables and descriptive statistics (M = mean, SD = standard deviation) for the quantitative variables. Pearson's chi-squared tests were used to determine if there were significant differences at the 0.05 level between the frequencies of the categories in each group (sex, marital status, smoking, education, and physical activity). One-way ANOVA was used to determine if there were significant differences at the 0.05 level between the mean age and Body Mass Index (BMI) of the participants in each group.

Error bar charts were constructed to display the variations in the mean measures of Fasting Blood Glucose, Two Hour Postprandial Blood Glucose, Systolic Blood Pressure, Diastolic Blood Pressure, and Haemoglobin A1c ± 95% confidence intervals (CI) in each group on four occasions during the 90-

day study period, from Week 1 (baseline), through Weeks 4, 8 and 12 (endpoint).

The temporal changes in the clinical measures (Week 12 minus Week 1) were taken as the outcomes. The descriptive statistics changes (M ± 95% CI) were computed for each group. Negative mean values indicated that the levels declined between Week 1 and Week 12. Sample t-tests were conducted to determine if the mean changes in Fasting Blood Glucose, Two Hour Postprandial Glucose, Systolic Blood Pressure, Diastolic Blood Pressure, and Haemoglobin A1c between Week 1 and Week 12 were significantly different from zero at the 0.05 level in each group. The effect sizes were indicated by Cohen's *d*. The interpretation of Cohen's *d* was:

- < 0.3 = small
- Between 0.3 and 0.8 = moderate
- > 0.8 = large.

A matrix of correlation coefficients (Pearson's *r*) was constructed to identify significant correlations at the 0.05 level between changes in the clinical measures from Week 1 to Week 12 (Fasting Blood Glucose, Two Hour Postprandial Glucose, Blood Pressure and HbA1c), and the selected demographic and physical characteristics of the 75 cases (age, BMI and diabetic history), which could potentially be associated with the symptoms of type 2 diabetes.

Chapter 4 Results

4.1. Introduction

The results are presented in three main sections. Section 4.2 presents the results for Trial 1, with the results of statistical tests to determine the effects of the three modified diets (see chapter 3) on the blood glucose profile and blood pressures of the diabetic patients. Section 4.3 presents the results for Trial 2, with the results of statistical tests to determine the effects of the three prescribed diets on the blood glucose profile of the healthy participants. Section 4.4 presents the combined results of Trial 1 and 2, to compare the effects of the three prescribed diets between the diabetic patients and the healthy participants. Section 4.5 provides an overall summary of the results.

4.2. Trial 1 (Diabetic Patients)

4.2.1. Characteristics of Diabetic Patients

Table 4.1 summarizes the baseline characteristics of the diabetic patients in Week 1. The majority of the patients (48, 64.0%) were female. They ranged in age from 25 to 60 years (M = 48.88, SD = 8.12). Their duration of diabetes ranged from 1 to 25 years (M = 6.39, SD = 4.64). The majority (51, 68.0%) were married. The BMIs of the diabetics ranged from 21.67 to 47.38 kg/m^2 (M = 27.67, SD = 3.79). 76% were classified as either overweight (36, 48.0%) with BMI = 25.0 to 30 kg/m^2 or obese (21, 28.0%) with BMI > 30 kg/m^2.

The majority (50, 66.7%) of the diabetics did not smoke. The educational levels of the participants ranged from illiterate (9, 12.0%) to undergraduate (15, 20.0%). The most frequent educational level was high school (25, 33.3%). The majority of the diabetics (45, 60.0%) reported that their frequency of physical activity was “Never”. Of those undertaken physical activity only (7, 9.3%) achieved this daily.

Table 4.1. Characteristics of Diabetic Patients

Characteristics		Group			Total
		D-AJ (*n* = 25)	D-D (*n* = 25)	D-NS (*n* = 25)	
Sex	Female	16	17	15	48
		21.30%	22.70 %	20.0%	64.0%
	Male	9	8	10	27
		12.0%	10.70 %	13.30%	36.0%
Age (Years)	*M*	51.24	47.32	48.08	48.88
	SD	6.83	8.62	8.12	8.12
Duration of Diabetes	*M*	8.64	4.64	5.88	6.39
	SD	5.99	3.33	3.27	4.64
Marital Status	Married	18	17	16	51
		24.0%	22.7%	21.3%	68.0%
	Single	2	4	2	8
		2.7%	5.3%	2.7%	10.7%
	Divorced or Widow	5	4	7	16
		6.7%	5.3%	9.3%	21.3%
BMI (kg/m^2)	*M*	27.94	28.46	26.62	27.67
	SD	4.39	3.87	2.86	3.79
Smoking	No	17	18	15	50
		22.7%	24.0%	20.0%	66.7%

	Yes	8	7	10	25
		10.7%	9.3%	13.3%	33.3%
Education	Illiterate	3	2	4	9
		4.0%	2.7%	5.3%	12.0%
	Primary	9	12	5	26
		12.0%	16.0%	6.7%	34.7%
	High School	10	6	9	25
		13.3%	8.0%	12.0%	33.3%
	Under-graduate	3	5	7	15
		4.0%	6.7%	9.3%	20.0%
Physical activity	Never	15	11	19	45
		20.0%	14.7%	25.3%	60.0%
	Once/week	3	7	3	13
		4.0%	9.3%	4.0%	17.3%
	Twice/week	5	3	2	10
		6.7%	4.0%	2.7%	13.3%
	Daily	2	4	1	7
		2.7%	5.3%	1.3%	9.3%

Significance tests were conducted to determine if the characteristics of the diabetics were equivalent across the three groups. The frequencies of males and females did not vary significantly between the groups (χ^2 (2) = 0.35, p = .841). ANOVA indicated no statistically significant difference in the mean age across the groups (F (2, 72) = 1.73, p = .184); however, there was a significant difference between their duration of diabetes (F (2, 72) = 5.44, p < .001). ANOVA indicated no significant difference in the mean BMI across the groups (F (2, 73) = 1.63, p = .202). Marital status did not vary significantly between the

groups (χ^2 (4) = 1.99, p = .177). The frequencies of smokers and non-smokers did not vary significantly between the groups (χ^2 (2) = 0.84, p = .657). The frequencies of the four educational levels did not vary significantly between the groups (χ^2 (6) = .406, p = .379). The frequencies of the four levels of physical activity did not vary significantly between the groups (χ^2 (6) = 7.99, p = .238). Statistical evidence is provided to conclude that all but one of the characteristics of the patients were equivalent across the three groups. The mean duration of diabetes in the D-D group was significantly lower (p < .05) than the mean duration of diabetes in the D-AJ and D-NS groups. Consequently, the three groups were not equivalent in terms of their history of diabetes.

Table 4.2 below presents a matrix of correlation coefficients (Pearson's r) between the clinical measures at the baseline (week 1) and the age, BMI, and duration of diabetes of the patients. These correlations could potentially be associated with the symptoms of Type II diabetes. FBG was positively correlated with 2hpp (r = .887, p < .001) and HbA1c (r = .588, p < .001). 2hpp was positively correlated with DBP (r = .270, p = .019) and HbA1c (r =. 569, p < .001). SBP and DBP were positively correlated (r = .440, p < .001). Age was positively correlated with HbA1c (r = .231, p = .048); BMI (r = .312, p = .006); and duration of diabetes (r = .253, p = .028).

Table 4.2. Correlations between Clinical Measures and Participant Characteristics

	FBG	2hpp	SBP	DBP	HbA1c	Age	BMI	Duration
FBG	1							
2hpp	.887*	1						
SBP	.083	.070	1					
DBP	.188	.270*	.440*	1				
HbA1c	.588*	.569*	.199	.366*	1			
Age	-.021	-.004	.042	-.124	.231*	1		
BMI	.038	.059	-.002	-.020	.001	.312*	1	
Duration	.114	.151	-.048	.028	.199	.253*	.162	1

*Note: * Significant correlation ($p < .05$), Note: FBG = Fasting Blood Glucose; 2hpp = Two Hour Postprandial Glucose; SBP = Systolic Blood Pressure; DPB = Diastolic Blood Pressure; HbA1c = Haemoglobin A1c; Age = Age of participant (Years); BMI = Body Mass Index (kg/m^2); Duration = Duration of Type 2 Diabetes (Years)*

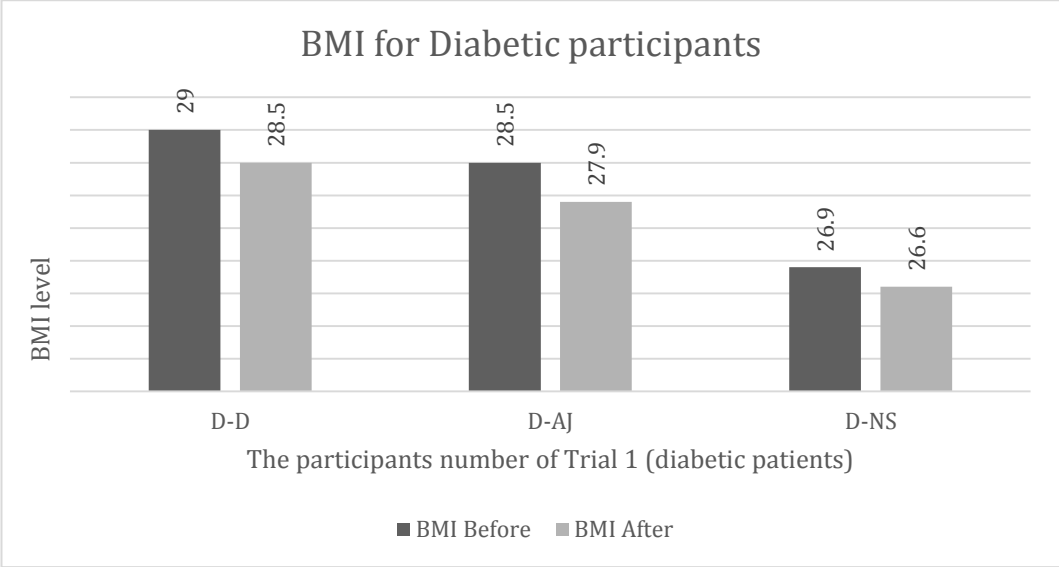


Figure 4.1. Body Mass Index BMI of the diabetic participants

Result in figure 4.1 shows that the BMI for Groups D-D, D-NS and D-AJ all decreased slightly over the 12 weeks of the study. All participants were categorized as overweight, BMI >25. The BMI was calculated using the patient's information height and weight) taken by the nurse at the clinic.

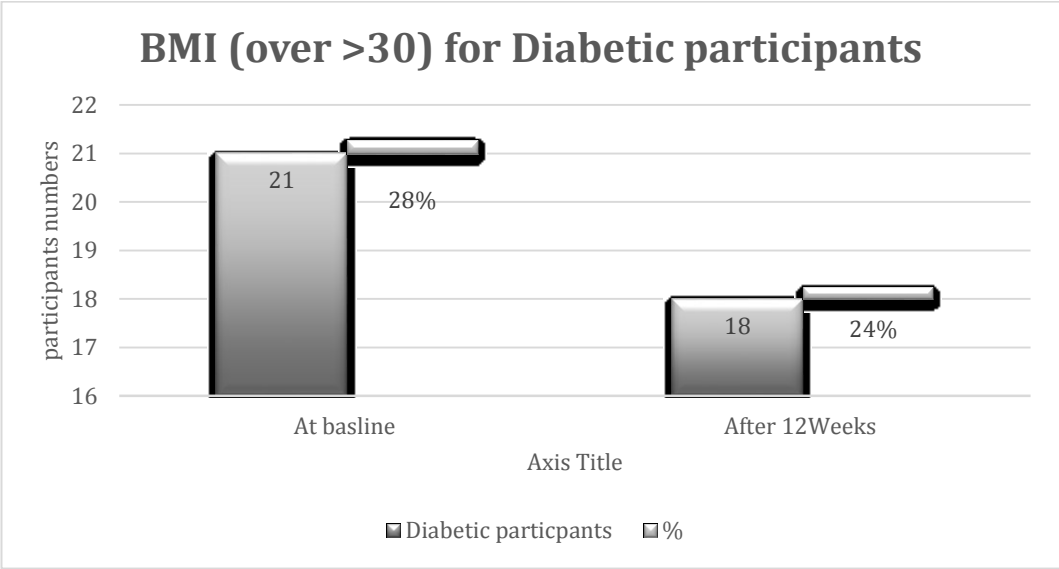


Figure 4.2. BMI (obesity level) of the diabetic participants

Figure 4.2 illustrates that the total percentage of diabetic patients who were obese (n= 21, 28%) at the beginning of the study and it was decreased at the end with (n=18, 24%).

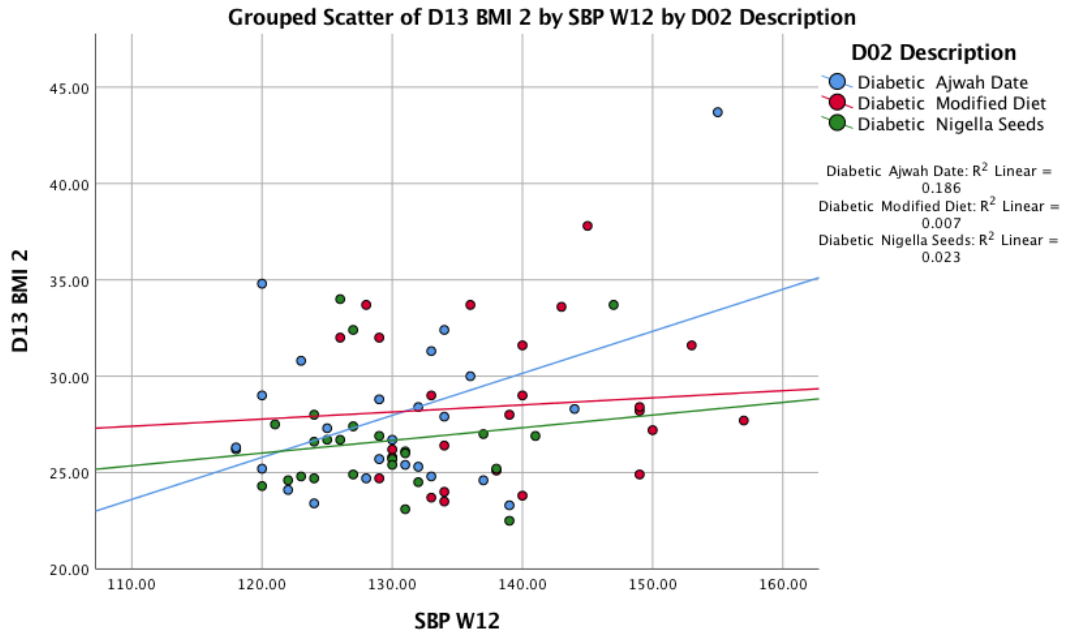


Figure 4.3. The correlation coefficient for BMI after treatment of dietary factors (*Nigella sativa*, Ajwa dates and modified diet group) of the diabetic participants and SBP

The figure 4.3 above shows a matrix of correlation coefficient (Pearson's *r*) between the BMI for the diabetic patients and the SBP measurement at the end of the treatment of Ns, AJ and modified diet. It has been shown that BMI for the AJ group has a strong correlation with SBP and there was significant decreased after 12 weeks of AJ intake ($r = 0.186$, $p < 0.05$). This correlation indicated an association between the reduction in blood pressure and in the BMI after treatment with AJ dates for 12 weeks. However, there was a weak correlation between the decreased BMI for the Ns and modified diet groups and SBP with $r = 0.023$ and $r = 0.007$ respectively.

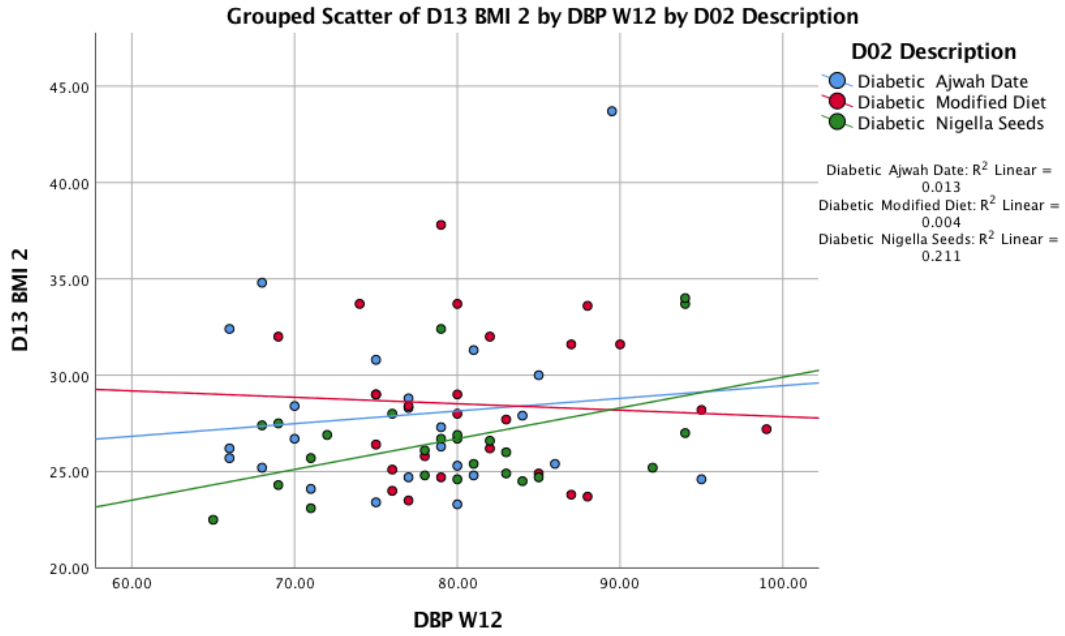


Figure 4.4.The correlation coefficient for BMI after (12 weeks) treatment of dietary factors (*Nigella sativa*, Ajwa dates and modified diet) of the participants and DBP

Figure 4.4 demonstrates the correlation between BMI and DBP for the diabetic group. BMI was positively correlated with DBP for *Nigella sativa* group (r = .211, p = 0.05) and the correlation is significant at the 0.05 level. However, there is a non-significant correlated between DBP and BMI for AJ and modified group with (r =0. 013, p .293) and (r =0.004, p .338) respectively.

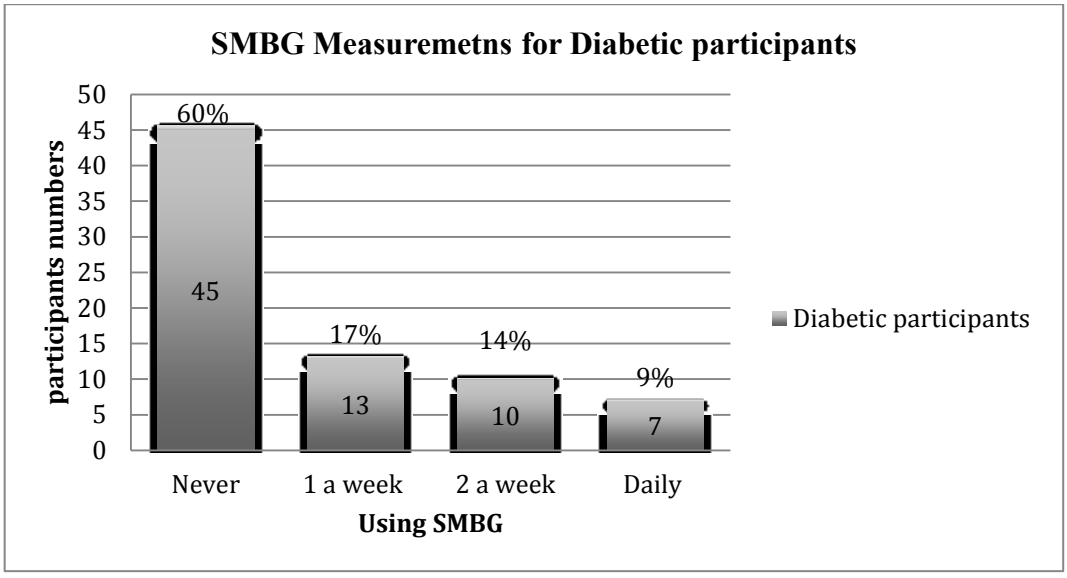


Figure 4.5. Measuring self-monitoring Blood Glucose (SMBG)

The given figure 4.5 provides the percentages of the self-monitoring blood glucose levels that were taken in the homes of diabetic participants. Based on the bar chart above (figure 4.5), most of the diabetic patients (60%) never measured the blood glucose level at home, while 17% of the diabetic patients measured BGL once a week , 14% of the diabetic participants measured their BGL twice a week and only 9 % self-monitored their BGL daily.

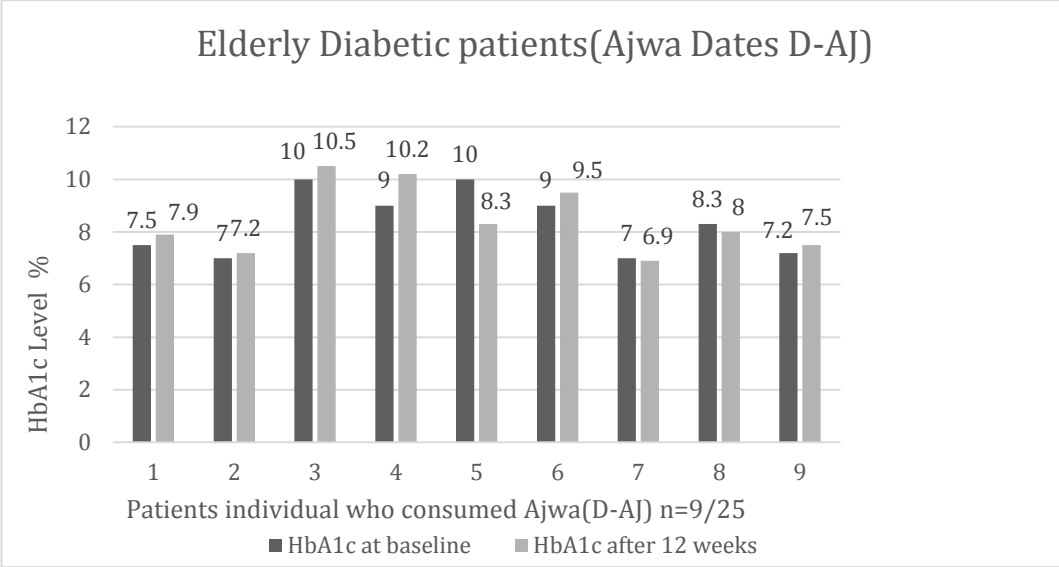


Figure 4.6: Distribution of HbA1c in elderly diabetic patients who had long duration of diabetes

Figure 4.6 shows the results from the analysis of HbA1c of patients with a long duration of diabetes to establish whether there could have been a possible link between the duration of diabetes and HbA1c levels. Only patient number 5 and 8 had a little decline in the HbA1c after 12 weeks of consuming Ajwa who were elderly and had a long duration (10 years to 20 years) of T2DM. It can be seen from figure 4.6, the HbA1c at the baseline (before the treatments) of diabetic patients who had long duration (> 10 years) happened in older subjects, who had lower levels of HbA1c after 12 weeks of Ajwa dietary intake.

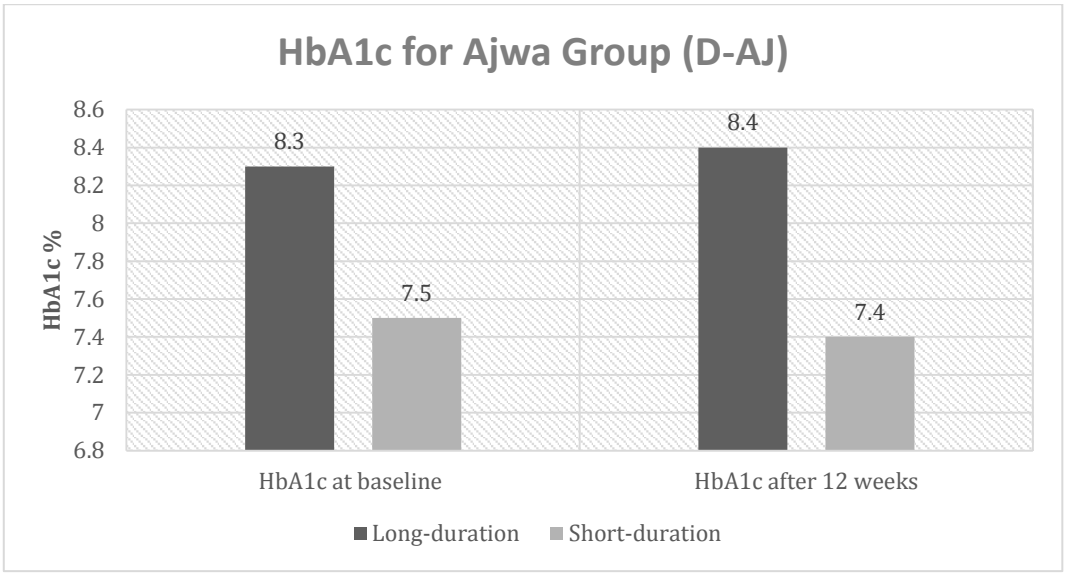


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Figure 4.7. Distribution of HbA1c in short-duration and long-duration sub-group for diabetic patients who had Ajwa date

The figure 4.7 demonstrates the HbA1c levels for the diabetic patients who had short-duration diabetes subgroup (less than 10 years) and the sub-group (who had long duration and elderly members). It can be seen from the figure above that by taking away the elderly people who had long duration (>10 years) had a positive decline in HbA1c level and the mean of HbA1c for the sub-group was higher after 12 weeks from Ajwa dietary intake.

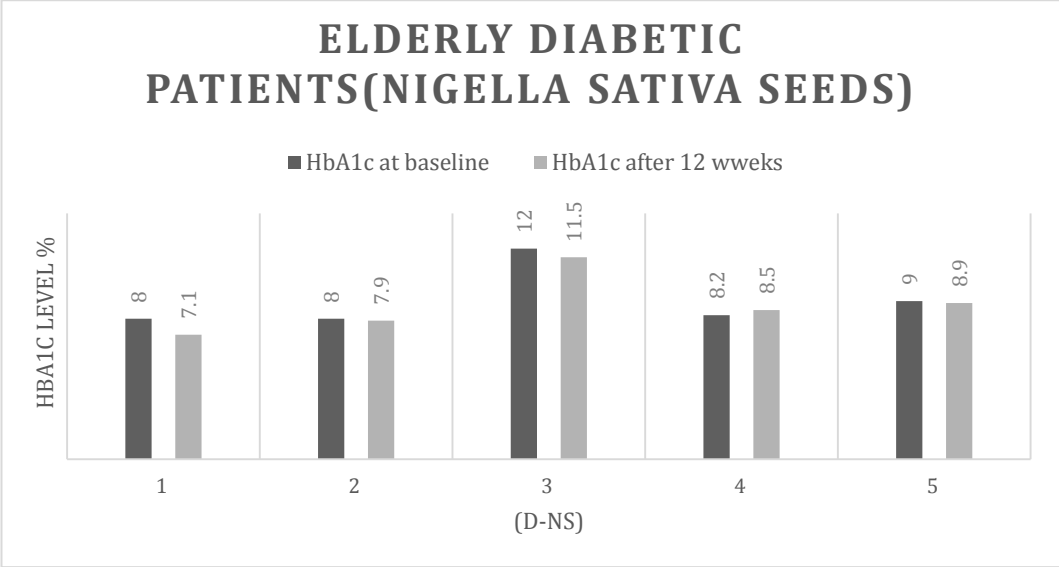

Figure 4.8. Distribution of HbA1c in elderly diabetic patients who had long duration of diabetes (*Nigella sativa* seeds)

Figure 4.8 demonstrates the sub-group (who were elderly and had a long duration of DM). As is observed from the bar chart 4.8, five participants out of the whole *Nigella sativa* group, D-NS (n=25) had long duration (more than 10 years) of diabetes. Only one patient (4) had an increase in the HbA1c levels after 12 weeks (8.5) of treatment with 2g/daily of *Nigella sativa* seeds. However, the other four participants showed a slight decrease in their HbA1c level after consuming *Nigella sativa* seeds for 12 weeks.

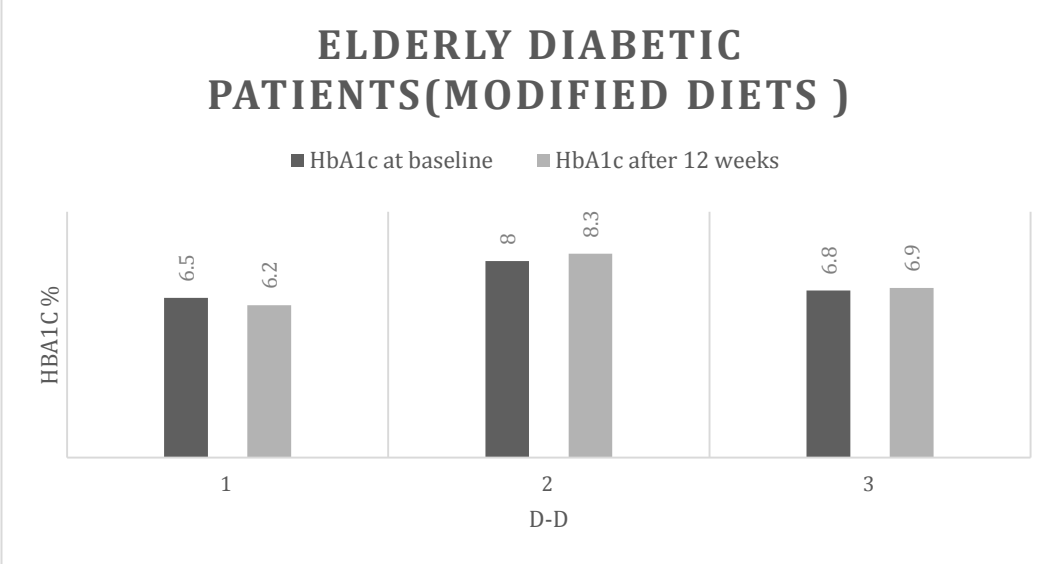

Figure 4.9. Distribution of HbA1c in elderly diabetic patients who had long duration of diabetes (Modified diet)

The given bar chart above (4.9) shows the HbA1c level of older patients, who had long duration (>10 years) of DM and had the modified diet. As presented in the figure 4.9, only two patients of the sub group had a slight rise in their HbA1c level after 12 weeks of following the modified diet

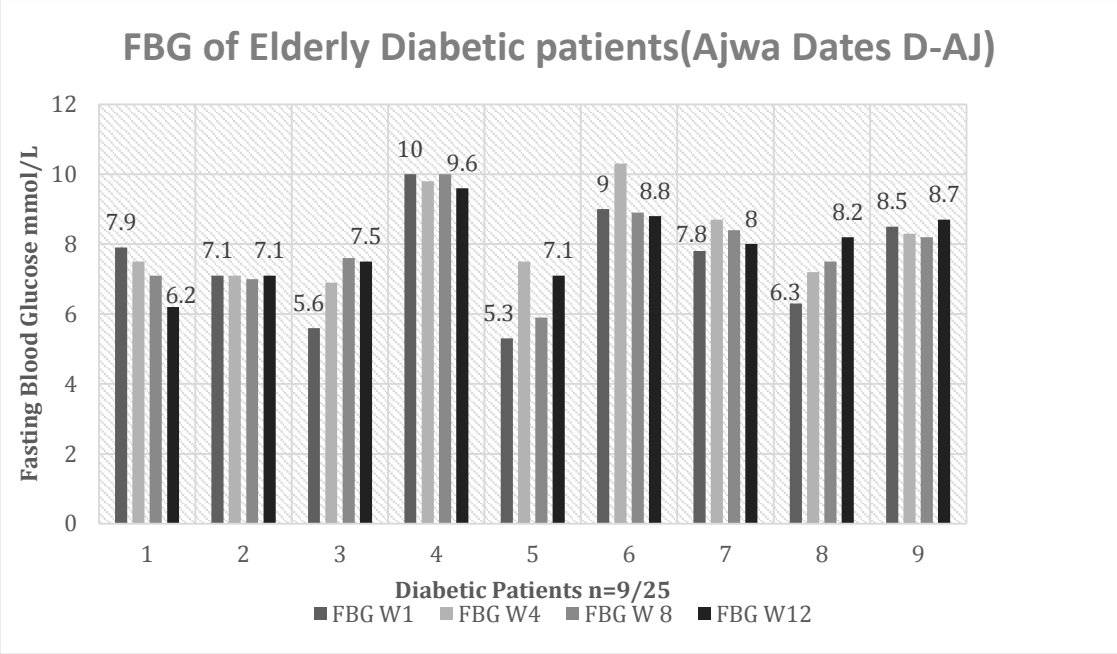

Figure 4.10. Distribution of FBG in elderly diabetic patients who had long duration of diabetes (Ajwa dates group)

The graph 4.10 shows the level of fasting blood glucose (FBG), for elderly participants who had long duration of diabetes (>10 years). Overall, most of the diabetic patients who consumed an Ajwa date daily showed an increase in their FBG levels at 12 weeks. Otherwise, only one patient had an improvement in the FBG levels from week 1(7.9 mmol/L) until week 12 (6.2 mmol/L). However, in some diabetic participants (4 and 6), the level of FBG is slightly low starting from 10 and 9 mmol/L at week 1 to 9.6 and 8.8 mmol/L at week 12 respectively. In conclusion, it seems that more than six patients from the elderly who had long duration of diabetes had an increase in FBG levels from week 1 until week 12.

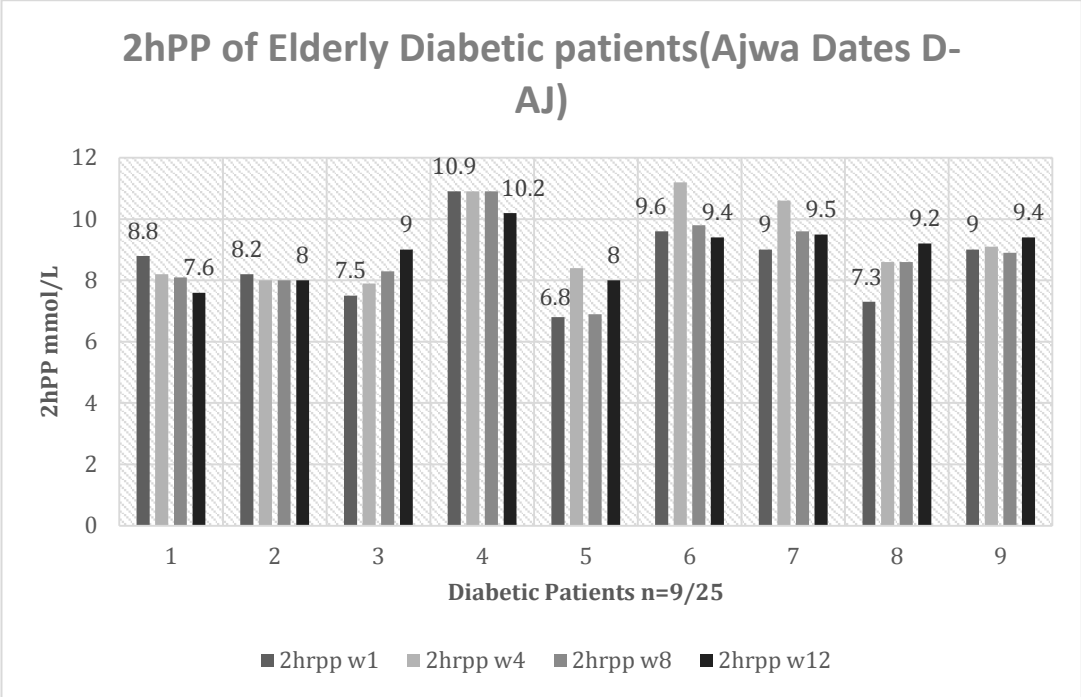

Figure 4.11. Distribution of FBG in elderly diabetic patients who had long duration of diabetes (Ajwa dates group)

The graph 4.11 shows the level of 2 hours postprandial (2hPP) blood glucose levels, for elderly participants who had long duration of diabetes (>10 years). Overall, most of the diabetic patients who consumed an Ajwa date daily show an increase in the 2hPP levels at 12 weeks. Patient number 1 had an improvement in the 2hPP levels from week 1(8.8 mmol/L) until week 12 (7.6 mmol/L). However, in some diabetic participants (2, 4 and 6), the level of 2hPP is slightly low starting from 8.2 , 10.9 and 9.35 mmol/L at week 1 to 8, 10.2 and 9.2 mmol/L at week 12 respectively. In conclusion, it seems that six diabetic patients from the elderly, who had long duration of diabetes, had an increase in FBG levels from week 1 until week 12.

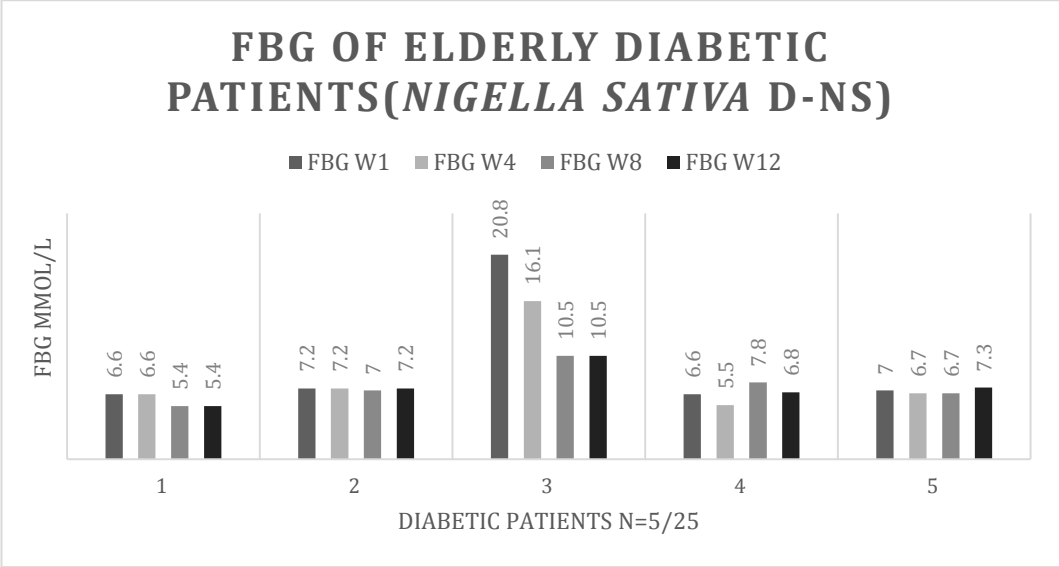

Figure 4.12. Distribution of FBG in elderly diabetic patients who had long duration of diabetes (*Nigella sativa* seeds)

The graph 4.12 shows the changes in the fasting blood glucose level of diabetic participants who had long duration of diabetes (>10 years). There are five elderly patients, who consumed 2 g/daily of *Nigella sativa* seeds. , Patients number 1 and 3 had a decline in the FBG levels from week 1(6.6 and 20.8 mmol/L) until week 12 (5.4 and 10.5 mmol/L) respectively. However, patient number 4 and 5 had a slight increase in FBG from week 1 (6.6 and 7 mmol/L) until week 12 (6.8 and 7.3 mmol/L).

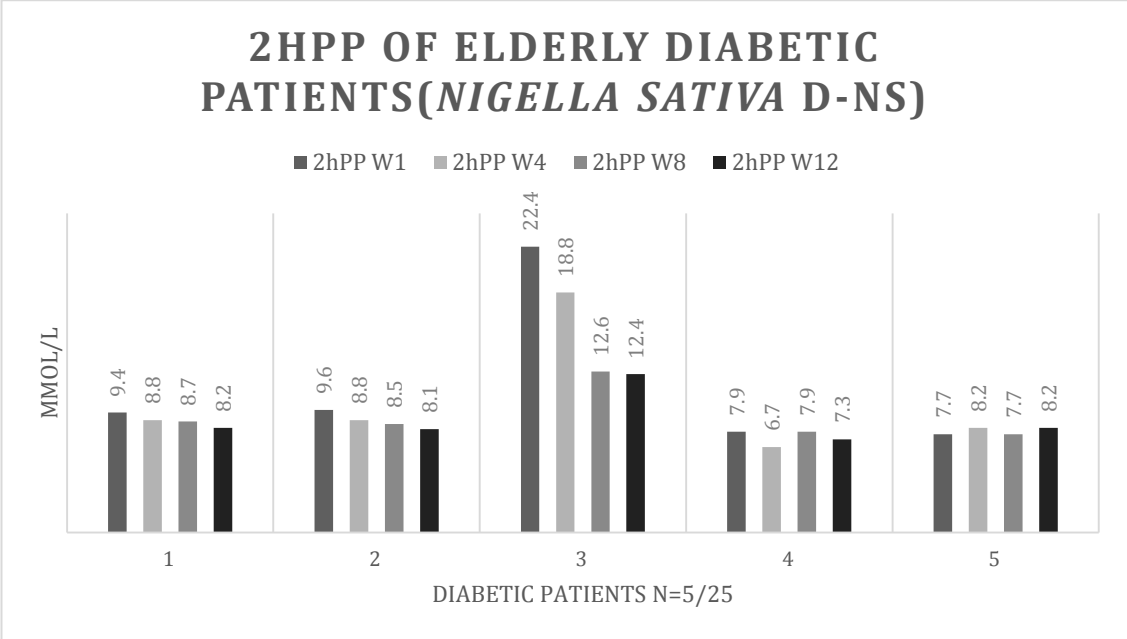

Figure 4.13. Distribution of 2hpp in elderly diabetic patients who had long duration of diabetes (*Nigella sativa* seeds)

The graph 4.13 demonstrates the changes in the 2 hours postprandial blood glucose of diabetic participants who had long duration of diabetes (>10 years). There were five elderly patients, who consumed 2 g/daily of *Nigella sativa* seeds. Patients number 1, 2, 3 and 4 had a decline in the 2hPP blood glucose level from week 1(9.4, 9.6, 22.4 and 7.9) until week 12 (8.2, 8.1, 12.4 and 7.3) respectively. However, only patient number 5 had a slight increase in 2hpp from week 1 (7.7 mmol/L) until week 12 (8.2 mmol/L).These data are confused by the results from patient 3 who seems on all these parameters to have a significantly worse condition than the other patients . Patient 3 however shows a significant improvement during the period of the study achieving values close to the other members of this cohort .

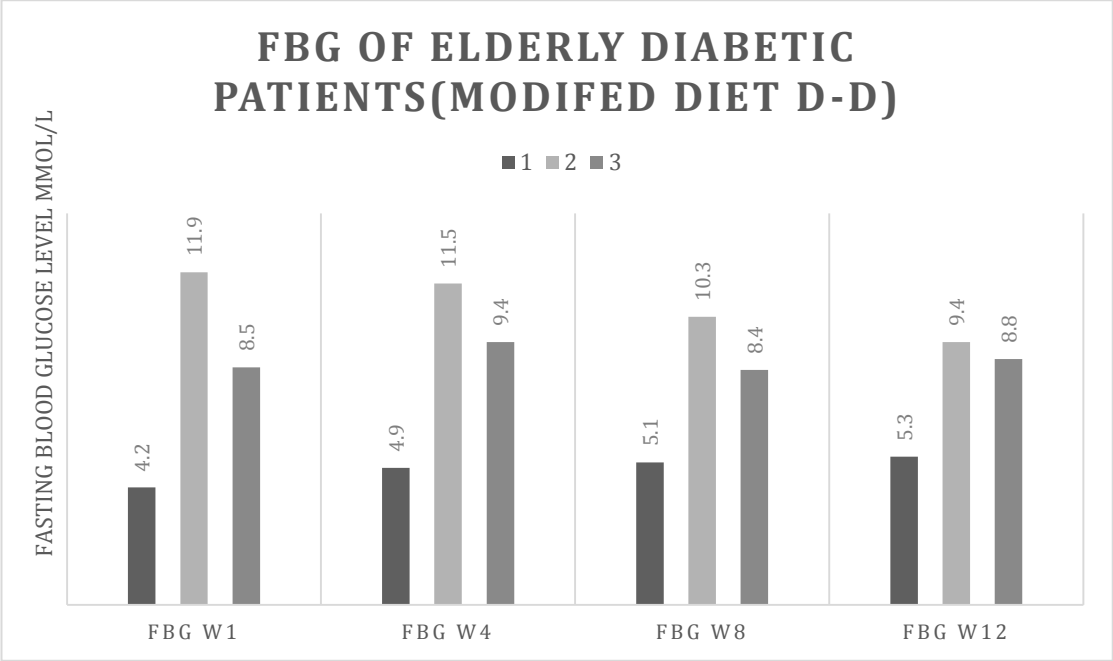

Figure 4.14. Distribution of FBG in elderly diabetic patients who had long duration of diabetes (Modified diet group)

Figure 4.14 shows changes in fasting blood glucose (FBG) levels for week 1 until week 12, for elderly diabetic subjects who had long duration of diabetes (>10 years). Patient number 2's FBG level declined from week 1(11.9 mmol/L) to week 12 (9.4 mmol/L). However, patient number 1 had a slight rise from week 1(4.2 mmol/L) until week 12 (5.3 mmol/L) but still maintained a fasting blood glucose level in the control average. Furthermore, in patient number 3, there is a small increase in week 4 (9.4 mmol/L) and 12 (8.8 mmol/L) while the starting FBG level was 8.5 mmol/L at week 1 and 8.4 mmol/L at week 8.

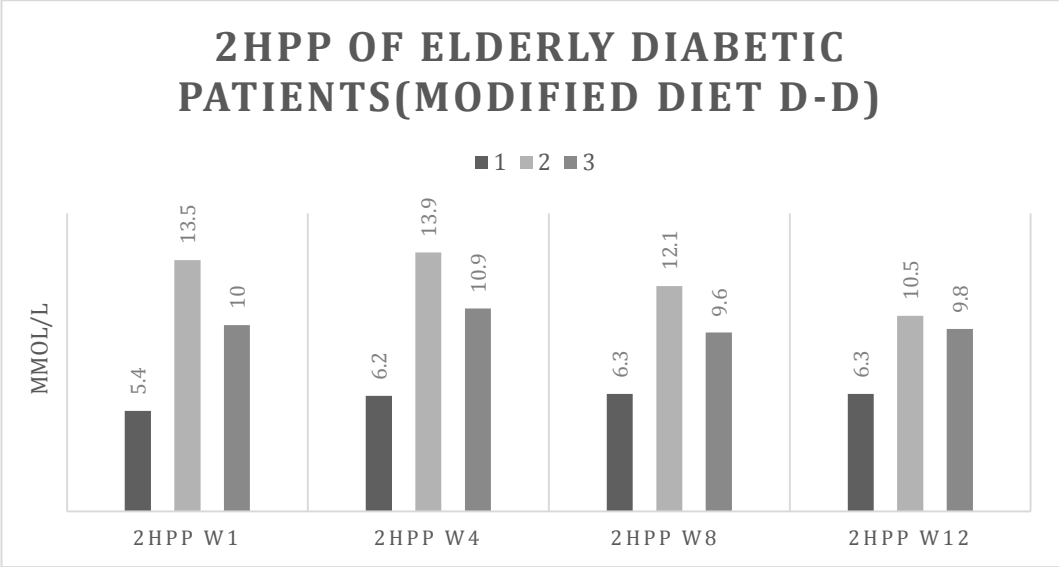

Figure 4.15. Distribution of 2hpp in elderly diabetic patients who had long duration of diabetes (Modified diet group)

The figure 4.15 shows changes in 2 hours postprandial blood glucose levels for week 1 until week 12, for elderly diabetic subjects who had long duration of diabetes (>10 years). Patient number 2's 2hpp declined from week 1(13.5 mmol/L) until week 12 (10.5 mmol/L). However, patient number 1 had a slight increase from week 1(5.4 mmol/L) until week 12 (9.8 mmol/L) but the 2 hours postprandial blood glucose levels were still within the average of the expected 2hpp levels. Furthermore, patient number 3 also had a slight increase in week 4 (10 mmol/L) and 12 (9.8 mmol/L). However, patient 3 started with a 2hpp level of 10.9 mmol/L at week 1 and 9.6mmol/L at week 8.

4.2.2. Blood Glucose Profile of Diabetic Patients

4.2.2.1. Fasting Blood Glucose (FBG) in Diabetic Patients

Figure 4.16 illustrates the variations in the mean levels of the repeated measures of Fasting Blood Glucose (FBG) ± 95% confidence intervals (CI) across the three groups of diabetic patients. The four repeated measures within each of the three groups were collected on Week 1 (baseline), through Weeks 4 and 8, to Week 12 (endpoint). The mean FBG levels of all patients remained consistently greater than seven mmol/L throughout Trial 1, reflecting their continuing diabetic condition (because FBG levels greater than seven mmol/L or higher on two separate tests are indicative of diabetes). In the D-AJ group, the mean FBG levels declined from 7.42 mmol/L in Week 1 to 7.27 mmol/L in Week 12. The mean FBG levels in the D-D group declined from 8.64 mmol/L in Week 1 to 7.71 mmol/L in Week 12. The mean FBG levels in the D-NS group declined from 8.24 mmol/L in Week 1 to 7.04 mmol/L in Week 12.

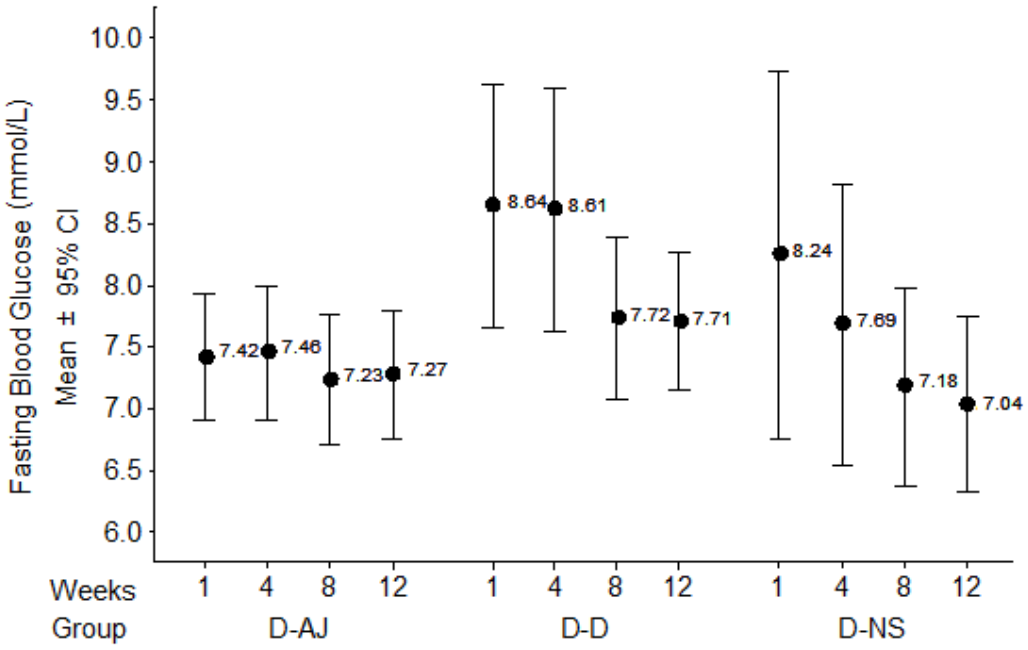

Figure 4.16. Repeated measures of FBG in Diabetic Patients

Table 4.3 presents the results of repeated measures ANOVA. This analysis was conducted to determine the extent to which the mean FBG of the diabetic patients varied within (a) duration and the interaction between duration x group; and (b) between the three groups. Applying $p < .05$ to reflect statistical significance, the results of ANOVA indicated that duration had a significant effect on the FBG levels (F (3, 216) = 13.24 ($p < .001$) but with a small effect size, indicated by Eta Squared (η^2) = .155. There was also a significant duration x group interaction (F (6, 216 = 2.20, p = .044) but with a smaller effect size (η^2 = .058). The direction of the effect was consistent in all three groups (i.e., the FBG declined over time). There was no significant difference between the FBG levels of the three groups (F (2, 72) = 1.36, p = .270) with an effect size η^2 = .036which is not clinically significant (i.e., < .04).

Table 4.3. Comparison of FBG across Duration and Groups in Diabetic Patients

Effect	Source of Variance	*df 1*	*df2*	*F*	*p*	Effect Size η^2
Within-subjects	Duration	3	216	13.24	<.001*	.155
	Duration x Group	6	216	2.20	.044*	.058
Between-subjects	Group	2	72	1.36	.270	.036

Note: * Significant difference ($p < .05$)

The conclusion is that no significant effects of the three dietary factors (i.e., the modified diet, the modified diet with Ajwa date, or the modified diet with *Nigella* seeds) could be detected between the FBG levels among the three groups of diabetic patients during Trial 1. The statistical evidence indicated, however, that the FBG levels did not remain constant, but fluctuated over time. There was a significant ordinal duration interaction, illustrated in Figure 4.14, because the FBG levels in the D-D and D-NS groups tended to decline more rapidly than in the D-AJ group.

4.2.2.2. Two Hours Post Prandial Glucose (2hpp) in Diabetic Patients

Figure 4.17 illustrates the variations in the mean levels of the repeated measures of Two Hours Post Prandial Glucose (2hPP) ± 95% CI across the three groups of diabetic patients throughout Trial 1. In the D-AJ group, the mean 2hPP levels varied from 8.39 mmol/L in Week 1 to 8.29 mmol/L in Week 12. The mean 2hPP levels in the D-D group decreased from 9.96 mmol/L in Week 1 to 8.70 mmol/L in Week 12. The mean 2hPP levels in the D-NS group decreased from 10.25 mmol/L in Week 1 to 8.29 mmol/L in Week 12. Two hours 2hpp above about 8 mmol/L is indicative of diabetes. The 2hPP levels of all the patients remained above eight mmol/L through Trial 1, reflecting their continuing diabetic condition.

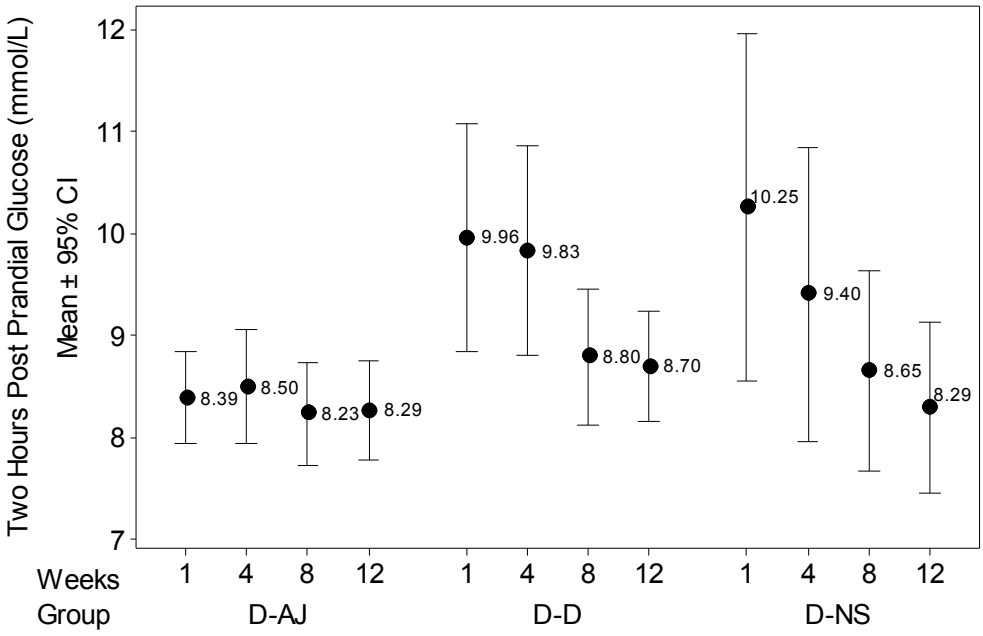

Figure 4.17. Repeated measures of 2hpp in diabetic patients

Table 4.4 presents the results of repeated measures ANOVA to determine the extent to which the mean 2hPP levels of the diabetic patients varied within (a) duration and the duration x group interaction; and (c) between the three groups of diabetic patients.

Table 4.4. Comparison of 2hpp across Duration and Groups in Diabetic Patients

Source of Variance	*df1*	*df2*	*F*	*P*	Effect Size η^2
Duration	3	216	21.42	<.001 *	.230
Duration x Group Interaction	6	216	4.44	<.001 *	.110
Group	2	72	1.51	.228	.040

Note: * Significant *(p* < .05)

The results of ANOVA indicated that time had a significant effect on the 2hPP levels (*F* (3, 216) = 21.42 (*p* < .001) but with a small effect size, indicated by η^2 = .233. There was also a significant duration x group interaction (*F* (6, 216 = 4.44, p = <.001) with a smaller effect size (η^2 = .110). This interaction was ordinal, because the direction of the changes in the mean values was consistent in all three groups (i.e., the 2hPP consistently declined over time). There was no significant difference between the 2hPP levels of the three groups *(F* (2, 72) = 1.51, *p* = .228) with aninsignificant effect size (η^2 = .040).

The conclusion is that the diets consumed by the three groups of diabetic patients did not have any significant effects on the differences between the mean 2hPP levels during Trial 1. The significant interaction indicated that the decline in 2hPP over time was more rapid in the D-D and D-NS groups than in the D-AJ group.

4.2.3. Glycated Haemoglobin (HbA1c) in Diabetic Patients

Figure 4.18 displays the variations (Mean ± 95% CI) in two repeated measures of Haemoglobin A1c (HbA1c) in each of the three groups of diabetic patients at the baseline and endpoint of the trial (Week 1 and 12).

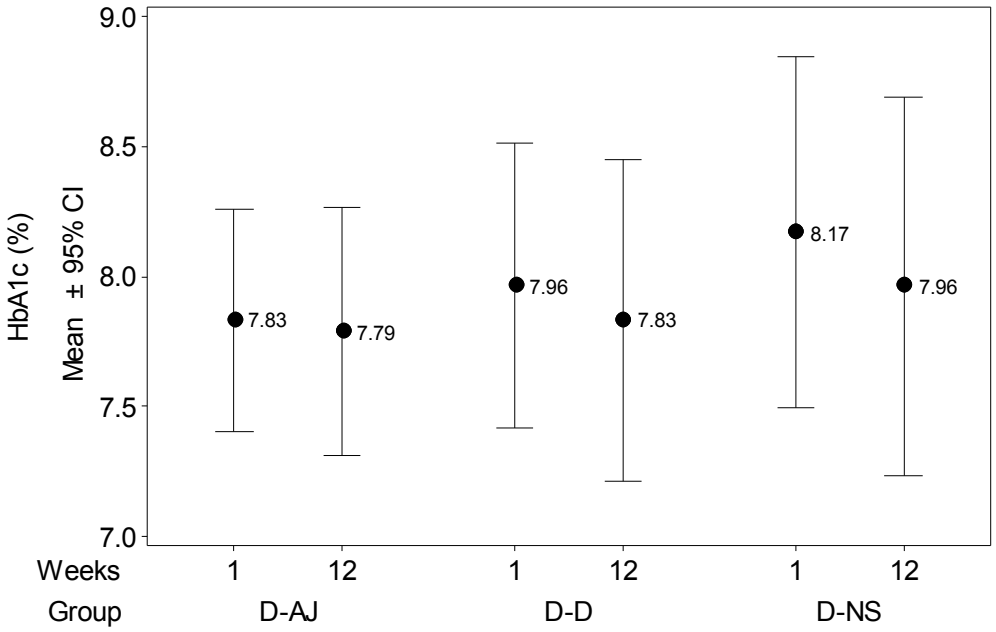

Figure 4.18. Repeated measures of HbA1c in diabetic patients

In the D-AJ group, the mean HbA1c declined from 7.83% in Week 1 to 7.79% in Week 12. The mean HbA1c in the D-D group decreased from 7.96% in Week 1 to 7.83% Week 12. The mean HbA1c in the D-NS group decreased from 8.17% in Week 1 to 7.96% in Week 12. The mean HbA1c levels were consistently elevated above the normal level expected in healthy persons (5%) and were typical of the levels of HbA1c observed in diabetics (over 7.0%). Table 4.5 presents the results of repeated measures ANOVA to determine the extent to which the mean HbA1c levels of the diabetic patients varied within (a) duration and the (c) the duration x group interaction); and between the three groups of diabetic patients.

Table 4.5. Comparison of HbA1c across Duration and Groups in Diabetic Patients

Effect	Source of Variance	df1	df 2	F	P	*Effect Size* η^2
Within-subjects	Duration	1	72	3.22	.077	.043
	Duration x Group	2	72	0.43	.653	.012
Between-subjects	Group	2	72	0.22	.805	.006

The results of ANOVA indicated that time had no significant effect on the HbA1c levels (F (1, 72) = 3.22 (p = .077) with a very small effect size (η^2 = 043). There was no significant duration x group interaction (F (2, 72 = 0.43, p = .653) with an even smaller effect size (η^2 = .012). There was no significant difference between the HbA1c levels of the three groups (F (2, 72) = 0.22, p = .805) with a clinically insignificant effect size (η^2 = .006).

The conclusion is that the different diets consumed by the three groups of diabetic patients had no significant effects on the differences between the mean levels of HbA1c of the patients during Trial 1. Furthermore, time also had no significant effects.

4.2.4. Blood Pressure in Diabetic Patients

4.2.4.1. Systolic Blood Pressure (SBP) in Diabetic Patients

Figure 4.19 illustrates the variations (Mean ± 95% CI) in the repeated measures of SBP across the three groups of diabetic patients in Weeks 1, 4, 8, and 12.

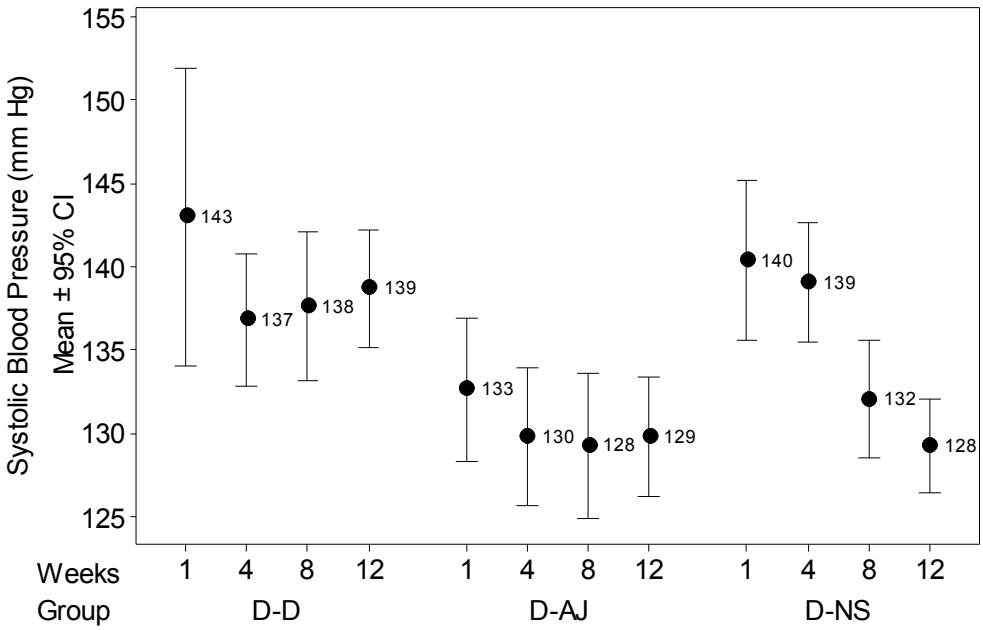

Figure 4.19. Repeated measures of SBP in diabetic patients

In the D-D group, the mean SBP varied from 143 in Week 1 to 139 in Week 12. The mean SBP in the D-AJ group decreased from 133 in Week 1 to 129 in Week 12. The mean SBP the D-NS group declined more rapidly from 140 in Week 1 to 128 in Week 12. A systolic blood pressure of 140 or higher, on repeated measurements, is considered hypertension, or high blood pressure. The upper bounds of the 95% CIs were above 140 in Week 1 and 2, implying some patients had hypertension, but thereafter the upper bounds of the CIs were below 140, implying that hypertension was relieved. Referring to figure 4.3 it can be seen that there is a positive relation between BMI and reducing the blood pressure due to the decrease the BMI obesity level during 12 weeks at the end of the study especially for Ajwa group

Table 4.6 presents the results of repeated measures ANOVA. Time had a significant effect on the SBP (F (3, 216) = 9.16 (p < .001) but with a small effect size (η^2 = .233). There was also a significant duration x group interaction (F (6, 216) = 3.17, p = .005) with a smaller effect size (η^2 = .018). The duration x group interaction was disordinal. Figure 4.17 displays that the changes in the SBP were not consistently in the same direction in the three groups. The mean SBPs declined rapidly over time in group D-NS, decreased followed by an increase in group D-D, but remained consistently low in group D-AJ. The significant difference between the SBP of the three groups (F (2, 72) = 6.08, p = .004) with an insignificant effect size (η^2 = .144) could not be interpreted because the effects of diet on SBP in Trial 1 were inconsistent.

Table 4.6. Comparison of SBP across duration and Groups in Diabetic Patients

Effect	Source of Variance	*df1*	*df2*	*F*	*P*
Within-subjects	Duration	3	216	9.61	<.001*
	Duration x Group	6	216	3.17	.005*
Between-subjects	Group	2	72	6.08	.004*

Note: * Statistically significant (p < .05)

4.2.4.2. Diastolic Blood Pressure (DBP) in Diabetic Patients

Figure 4.20 illustrates the variations (Mean ± 95% CI) in the repeated measures of Diastolic Blood Pressure (DBP) in the three groups of diabetic patients in Weeks 1, 4, 8 and 12. In the D-AJ group, the mean DBP declined from 83 in Week 1 to 77 in Week 12. The mean DBP in the D-D group varied from 82 in Week 1 to 81 in Week 12. The mean DPB in the D-NS group declined from 87 in Week 1 to 79 in Week 12. A diastolic blood pressure of 90 or higher, on repeated measurements, is considered to indicate hypertension, or high blood pressure; however, all of the repeated of DBP measures were less than 90. The results of repeated measures ANOVA are presented in Table 4.7.

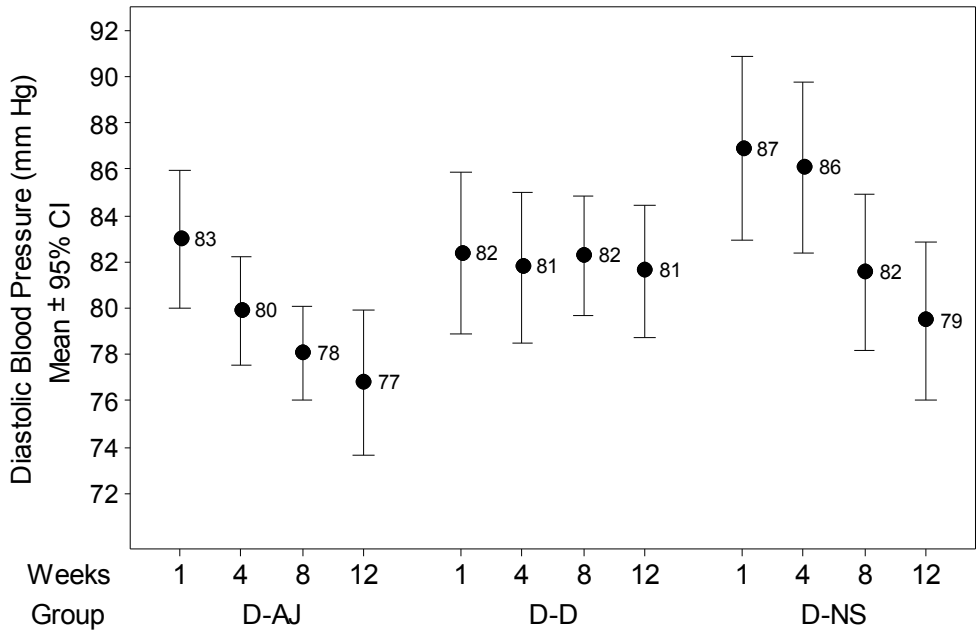

Figure 4.20. Repeated measures of DPB in diabetic patients

Table 4.7. Comparison of DBP across duration and Groups in Diabetic Patients

Effect	Source of Variance	*df1*	*df 2*	*F*	*P*	Effect Size η^2
Within-subjects	Duration	3	216	14.26	<.001*	.295
	Duration x Group	6	216	3.56	.005*	.094
Between-subjects	Group	2	72	2.61	.080	.068

Note: * Significant ($p < .05$)

Duration had a significant effect on the DBP (F (3, 216) = 14.26 ($p < .001$) with a moderate effect size (η^2 = .295). There was also a significant duration x group interaction (F (6, 216 = 3.56, p = .005) with a small effect size (η^2 = .094). This interaction was disordinal because figure 4.18 shows that DBP tended to decrease rapidly in the D-NS group, decrease less rapidly in the D-AJ group, but remain relatively constant in the D-D group. There was no significant difference between the DBP of the three groups (F (2, 72) = 2.61, p = .080) with

a very small effect size (η^2 = .068). The conclusion is that the disordinal interaction meant that the effects of diet on the DBP of the three groups of diabetics were inconsistent. The 2 groups taking supplements show a decline whilst those on the diet alone did not. It might be claimed that the 2 supplements produced a reduction in DBP, which was not seen in diet only patients. It would appear that supplementing the modified diet plus (Ajwa and *Nigella)* dose have effect on DBP. Referring to figure 4.4 it has been shown that there is correlation between reduced BMI level and blood pressure (DBP). The reduction in DBP for the groups D-NS and D-AJ is greater than for the D-D due to the high level of BMI in the modified diet group.

4.3. Trial 2: Healthy Participants

4.3.1. Characteristics of Healthy Participants

Table 4.8 summarizes characteristics of the healthy participants. The majority of the 75 healthy participants (47, 62.7%) were female, and they ranged in age from 20 to 60 years (*M* = 33.77, *SD* = 9.02). About one-half of them (37, 49.3%) were married. Their BMIs ranged from 18.61 to 37.02 kg/m^2 (*M* = 25.53, *SD* = 3.92). Over half were classified as either overweight (29, 38.7%) with BMI = 25.0 to 30 kg/m^2 or obese (10, 13.3%) with BMI > 30 kg/m^2. The majority (49, 65.3%) did not smoke. The educational levels of the participants ranged from primary (3, 4.0%) to postgraduate (18, 24.0%). The most frequent educational level was undergraduate (36, 48.0%). Over one third of the healthy subjects (26, 34.7%) reported that their frequency of physical activity was “Daily”. The least frequent level of physical activity (12, 16.0 %) was two or three times a week.

Statistical tests were conducted to determine if the characteristics of the healthy were equivalent across the three groups. The frequencies of males and females did not vary significantly between the groups (χ^2 (2) = 1.48, *p* = .477). ANOVA indicated no significant difference in the mean age across the groups (*F* (2, 72) = 1.73, *p* = .184). ANOVA also indicated a significant difference in the mean BMI between the groups (*F* (2, 72) = 3.83 *p* = .026). Marital status also varied significantly between the three groups (χ^2 (4) = 19.11, *p* = .001).

Table 4.8. Demographic and Contextual Characteristics of Healthy Participants

Characteristics		Group			Total
		C-AJ (*n* = 25)	C-D (*n* = 25)	C-NS (*n* = 25)	
Sex	Female	14 18.7%	15 20.0%	18 24.0%	47 62.7%
	Male	11 14.7%	10 13.3%	7 9.3%	28 37.3%
Age (Years)	*M*	30.72	30.12	40.48	33.77
	SD	6.74	4.99	10.49	9.02
Marital Status	Married	11 14.7%	11 14.7%	15 20.0%	37 49.3%
	Single	14 18.7%	14 18.7%	4 5.3%	32 42.7%
	Divorced or Widow	0 0.0%	0 0.0%	6 8.0%	6 8.0%
BMI (kg/m^2)	*M*	24.08	25.48	27.03	25.53
	SD	4.10	2.63	4.37	3.92
Smoking	No	16 21.3%	21 28.0%	12 16.0%	49 65.3%
	Yes	9 12.0%	4 5.3%	13 17.3%	26 34.7%
Education	Primary	0 0.0%	0 0.0%	3 4.0%	3 4.0%

	High School	4 5.3%	1 1.3%	13 17.3%	18 24.0%
	Under-graduate	14 18.7%	15 20.0%	7 9.3%	36 48.0%
	Post-graduate	7 9.3%	9 12.0%	2 2.7%	18 24.0%
Physical activity	Never	2 2.7%	0 0.0%	15 20.0%	17 22.7%
	Once/week	10 13.3%	4 5.3%	6 8.0%	20 26.7%
	Two to Three /week	4 5.3%	5 6.7%	3 4.0%	12 16.0%
	Daily	9 12.0%	16 21.3%	1 1.3%	26 34.7%

The frequencies of smokers and non-smokers also varied significantly between the groups (χ^2 (2) = 7.18, p = .028). The frequencies of the four educational levels also varied significantly between the groups (χ^2 (6) = 26.50, p <.001). Furthermore, the frequencies of the four levels of physical activity varied significantly between the groups (χ^2 (8) = 40.21, p < .001).The differences between the three groups could potentially influence their blood glucose profiles and blood pressures, thereby confounding the impact of the three prescribed diets.

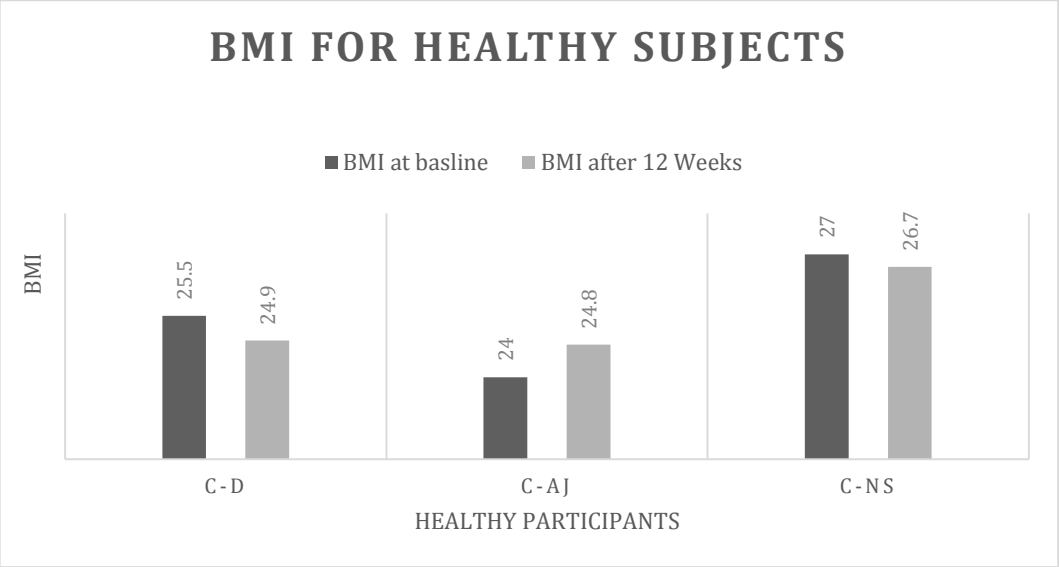

Figure 4.21. Body Mass Index BMI of the participants

Figure 4.21 above illustrates that of the 75 participants in the non -diabetic group, one third of them (C-D) had an average BMI of 25.5kg/m^2 before the study, which is considered to be overweight (since it is between 25-30 kg/m^2), but after the study this same group had an average BMI of 24.9, which is considered normal (since it is between 20-25 kg/m^2). The participants who followed the modified diet supplemented with *Nigella sativa* seeds (C-NS) had an average BMI of 27 kg/m^2 before the study, which came down to 26.7 kg/m^2 after the study. Furthermore, those who followed the modified diet supplemented with an Ajwa date appeared to have an average BMI before and after the study, 24 and 24.8 kg/m^2 respectively.

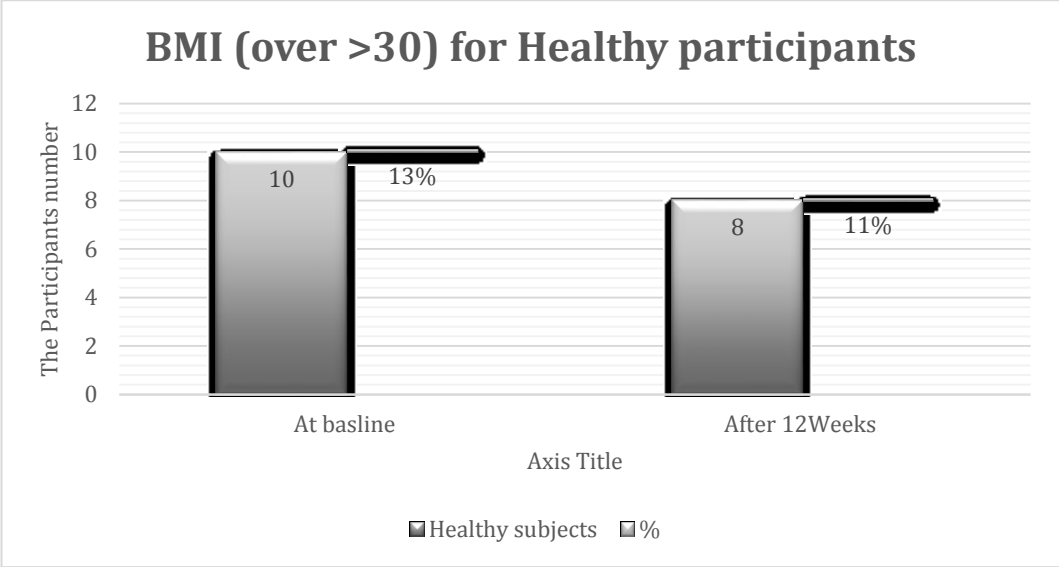

Figure 4.22. BMI (obesity level) of the Healthy participants

Figure 4.22 shows that 10 of the healthy participants (13%) were obese at the baseline at the study. By the end of the 12 weeks, after following either the modified diet, or the supplemented diet with either *Nigella sativa* seeds or Ajwa dates, the number of non-diabetic participants considered obese fell by 2 to 11%.

4.3.2. Blood Glucose Profile of Healthy Participants

4.3.2.1. Fasting Blood Glucose (FBG) in Healthy Participants

Figure 4.23 illustrates the variations in the mean levels of the repeated measures of Fasting Blood Glucose (FBG) ± 95% confidence intervals (CI) across the three groups of healthy subjects during Trial 2.

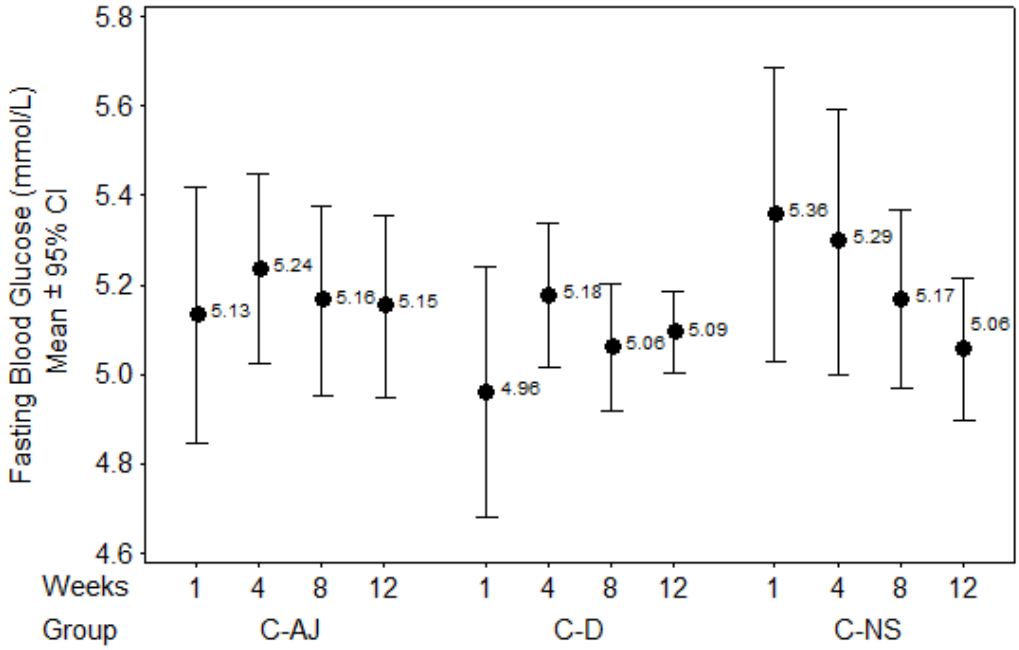

Figure 4.23 Repeated measures of FBG in healthy subjects

The mean FBG levels were consistently less than 5.6 mmol/L indicative of healthy individuals who did not have diabetes. In the C-AJ group, the mean FBG levels varied from 5.13 mmol/L in Week 1 to 5.15 mmol/L in Week 12. The mean FBG levels in the C-D group varied from 4.96 mmol/L in Week 1 to 5.09 mmol/L in Week 12. The mean FBG levels in the C-NS group varied from 5.36 mmol/L in Week 1 to 5.06 mmol/L in Week 12.

Table 4.9 presents the results of repeated measures ANOVA. There was no significant difference in the FBG levels within duration (F (3, 216) = 1.98 (p = .117) with nonsignificant effect size (η^2 = .027). There was no significant duration x group interaction (F (6, 216 = 1.73, p = .155) with a very small effect size (η^2 = .049). There was no significant difference between the FBG levels of the three groups (F (2, 72) = 0.68, p = .501) with an effect size that was not significant (η^2 = .019).

Table 4.9. Comparison of FBG across Duration and Groups in Healthy Subjects

Effect	Source of Variance	*df1*	*df2*	*F*	*p*	Effect Size η^2
Within-subjects	Duration	3	216	1.98	.117	.027
	Duration x Group	6	216	1.73	.115	.040
Between-subjects	Group	2	72	0.68	.501	.019

The conclusion is that the two dietary factors consumed by the three groups of healthy subjects did not have any significant effects on the differences between their mean FBG levels during Trial 2. The mean FBG levels remained constant over duration, and the changes in the FBG levels over duration were the same in the three groups, as illustrated in Figure 4.21.

4.3.2.2. Two Hours Post Prandial Glucose (2hpp) in Healthy Subjects

Figure 4.24 illustrates the variations in the mean levels of the repeated measures of 2hpp ± 95% CI across the three groups of healthy subjects during Trial 2. The 2hpp levels of all the patients remained below eight mmol/L between Week 1 and Week 12, indicating that they did not have diabetes. In the C-AJ group, the mean 2hpp levels varied from 5.66 mmol/L in Week 1 to 5.64 mmol/L in Week 12. The mean 2hpp levels in the C-D group varied from 6.27 mmol/L in Week 1 to 6.43 mmol/L in Week 12. The mean 2hpp levels in the C-NS group varied from 6.10 mmol/L in Week 1 to 5.60 mmol/L in Week 12.

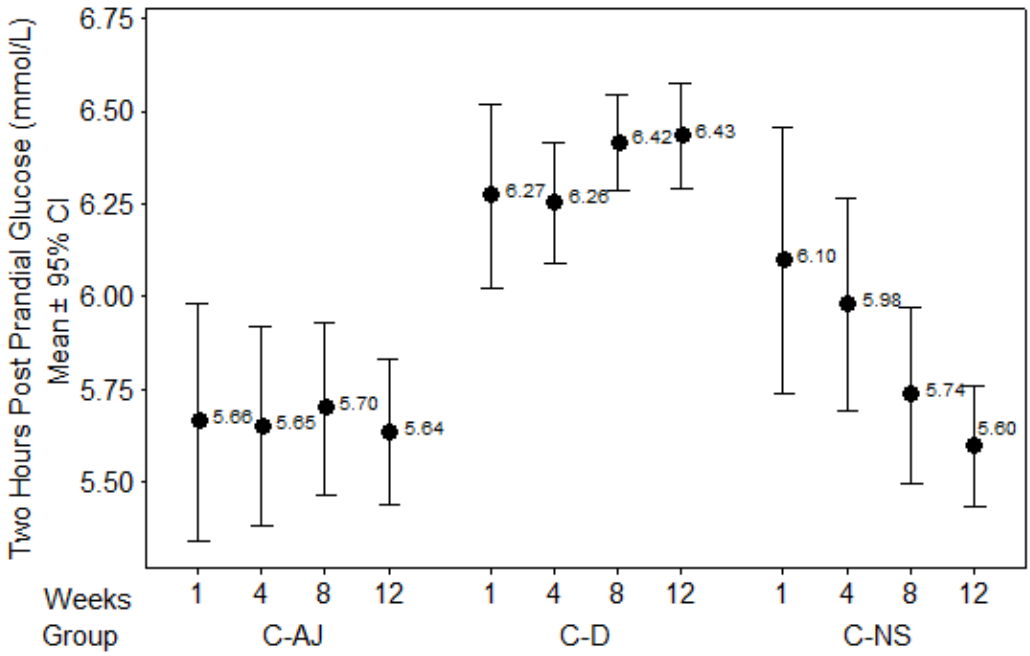

Figure 4.24. Repeated measures of 2hpp in healthy subjects

Table 4.10 presents the results of repeated measures ANOVA. The results indicated that duration had no significant effect on the 2hpp levels (F (3, 216) = 1.39 (p = .245) with an effect size that was not significant (η^2 = .019). There was, however, a significant duration x group interaction (F (6, 216 = 4.44 p < .001) with a small effect size (η^2 = .119). There was also a significant difference between the 2hpp levels of the three groups (F (2, 72) = 13.33, p <.001) with a moderate effect size (η^2 = .270).

Table 4.10. Comparison of 2hpp across Duration and Groups in Healthy Participants

Effect	Source of Variance	*df1*	*df2*	*F*	*P*	Effect Size η^2
Within-subjects	Duration	3	216	1.39	.245	.019
	Duration x Group	6	216	4.84	<.001*	.119
Between-subjects	Group	2	72	13.33	<.001*	.270

Note: * Significant *(p* < .05)

The duration x group interaction was disordinal, because the directions of the changes in the 2hPP levels over duration were not the same in the three groups. As illustrated in Figure 4.22, the 2hPP levels in the C-AJ group tended to remain relatively constant, whereas the 2hpp levels in the C-D group tended to increase, whilst in the C-NS groups the 2hPP levels tended to decline over duration. Because the interaction was disordinal, and the effects were both positive and negative, the significant differences between the three groups were not interpretable.

4.4. Comparison of Diabetic Patients and Healthy Participants

4.4.1. Participants Characteristics (Trial 1 and Trial 2)

The demographic and physical characteristics of the six groups of participants are summarized and compared in Table 4.11. The majority of the participants (95, 63.3%) were female. The frequencies of males and females in each group did not vary significantly across the six groups (Pearson's X^2 (5) = 1.866, p = .867). The participants ranged in age from 20 to 60 years (M = 41.33, 95% CI = 38.49, 43.16). ANOVA indicated a significant difference in the mean age between the six groups (F (5, 144) = 34.17, p < .001). The ages of the three diabetic groups (M = 47.32 to 51.24 years) were significantly higher than the ages of the three control groups (M = 30.12 to 40.48 years).

The majority of the participants (88, 58.7%) were married. The marital status of the participants varied significantly across the six groups (Pearson's X^2 (10) = 40.255, p < .001). The diabetic group contained the highest frequencies of married, widowed, and divorced participants. The health group contained the highest frequencies of single participants.

The BMIs of the participants ranged from 18.61 to 47.38 kg/m^2 (M = 26.85, 95% CI = 26.15, 27.56). The majority of the participants were classified as overweight (65, 43.3% with BMI = 25.0 to 30 kg/m^2) or obesity (31, 20.7% with BMI > 30 kg/m^2). ANOVA indicated a statistically significant difference in the mean BMI between the six groups (F (5, 144) = 5.186, p < .001). The mean BMIs of two case groups: D-AJ (M = 28.53 kg/m^2) and D-D (M = 29.08 kg/m^2) were significantly higher than mean BMIs in the other four groups (M = 24.08 to 27.04 kg/m^2).

Table 4.11. Characteristics of Six Groups of Participants

Characteristic		Group						Total
		C-AJ	C-D	C-NS	D-AJ	D-D	D-NS	
Sex	Female	14 9.3%	15 10.0%	18 12.0%	16 10.7%	17 11.3%	15 10.0%	95 63.3%
	Male	11 7.3%	10 6.7%	7 4.7%	9 6.0%	8 5.3%	10 6.7%	55 36.7%
Age (Years)	Mean	30.72	30.12	40.48	51.24	47.32	48.08	41.33
	SD	6.74	4.99	10.49	6.83	8.62	8.12	11.37
Marital Status	Married	11 7.3%	11 7.3%	15 10.0%	18 12.0%	17 11.3%	16 10.7%	88 58.7%
	Single	14 9.3%	14 9.3%	4 2.7%	2 1.3%	4 2.7%	2 1.3%	40 26.7%
	Divorced or Widow	0 0.0%	0 0.0%	6 4.0%	5 3.3%	4 2.7%	7 4.7%	22 14.7%
BMI (kg/m^2)	Mean	24.08	25.48	27.04	28.53	29.08	26.92	26.85
	SD	4.10	2.63	4.37	5.16	4.33	3.51	4.37
Smoking	No	16 10.7%	21 14.0%	12 8.0%	17 11.3%	18 12.0%	15 10.0%	99 66.0%
	Yes	9	4	13	8	7	10	51

		6.0%	2.7%	8.7%	5.3%	4.7%	6.7%	34.0%
Education	Illiterate	0 0.0%	0 0.0%	0 0.0%	3 2.0%	2 1.3%	4 2.7%	9 6.0%
	Primary	0 0.0%	0 0.0%	3 2.0%	9 6.0%	12 8.0%	5 3.3%	29 29.3%
	High School	4 2.7%	1 0.7%	13 8.7%	10 6.7%	6 4.0%	9 6.0%	43 28.7%
	Under-Graduate	14 9.3%	15 10.0%	7 4.7%	3 2.0%	5 3.3%	7 4.7%	51 34.0%
	Post-Graduate	7 4.7%	9 6.0%	2 1.3%	0 0.0%	0 0.0%	0 0.0%	18 12.0%
Physical activity	Never	2 1.3%	0 0.0%	15 10.0%	15 10.0%	11 7.3%	19 12.7%	62 41.3%
	Once/week	10 6.7%	4 2.7%	6 4.0%	3 2.0%	7 4.7%	3 2.0%	33 22.0%
	Twice/week	2 1.3%	2 1.3%	2 1.3%	5 3.3%	3 2.0%	2 1.3%	16 10.7%
	2 or 3 times/week	2 1.3%	3 2.0%	1 0.7%	0 0.0%	0 0.0%	0 0.0%	6 4.0%

	Daily	9	16	1	2	4	1	33
		6.0%	10.7 %	0.7%	1.3%	2.7%	0.7%	22.0 %

C-AJ (Control group consumed Ajwa date), C-D (Control group consumed Modified diet), C-NS (Control group supplemented with Nigella Seeds), D-AJ (Diabetes group consumed Ajwa dates), D-D (Diabetes group followed a modified diet) D-NS (diabetes group supplemented with Nigella sativa seeds) SD (standard deviation) BMI (Body mass Index)

A total of 51 (34.0%) of the participants were smokers. The frequencies of smokers and non-smokers in each group did not vary significantly across the six groups (Pearson's X^2 (5) = 8.111, p = .150). The educational levels of the participants ranged from illiterate (9, 6.0%) to postgraduate (18, 12.0%). The most frequent educational level (51, 34.0%) was undergraduate. The frequencies of the educational levels in each group varied significantly across the six groups (Pearson's X^2 (20) = 88.878, p <.001). The frequencies of the most highly educated participants (undergraduates and postgraduates) were higher in the healthy groups than in the diabetic groups.

The levels of physical activity of the participants ranged from "Never" (62, 41.3%) to "Daily" (33, 22.0%). The frequencies of the physical activity levels in each group varied significantly across the six groups (Pearson's X^2 (20) = 78.422, p <.001). Higher levels of physical activity were more frequent among the healthy subjects than the diabetic. Lower levels of physical activity were more frequent among the cases than the controls.

4.4.2 Blood Glucose Profile (Trial 1and2)

The results of repeated measures ANOVA using the data collected in Trial 1 and Trial 2 indicated that there were no significant differences between-subjects in the blood glucose profiles of the three groups of participants who consumed the two types of dietary factors. Consequently, the data for the three groups were pooled, in order to compare the blood glucose profiles of diabetic patients and healthy participants.

4.4.2.1 Fasting Blood Glucose (FBG)

Figure 4.25 illustrates the variations in the mean levels of FBG ± 95% CI in the three groups of healthy participants remained below 8 mmol/L between Week 1 and Week 12, indicating that they did not have diabetes. In contrast, the mean levels of FBG among the diabetic patients started above 8 mmol/L between Week 1 and Week 12, reflecting their diabetic condition. In both the healthy participants and the diabetic patients, the FBG levels tended to decline with duration. In the healthy participants, the mean FBG declined from 5.51 mmol/L in Week 1 to 5.10 mmol/L in Week 12. In the diabetic patients, the mean FBG declined from 8.10 mmol/L in Week 1 to 7.34 mmol/L in Week 12.

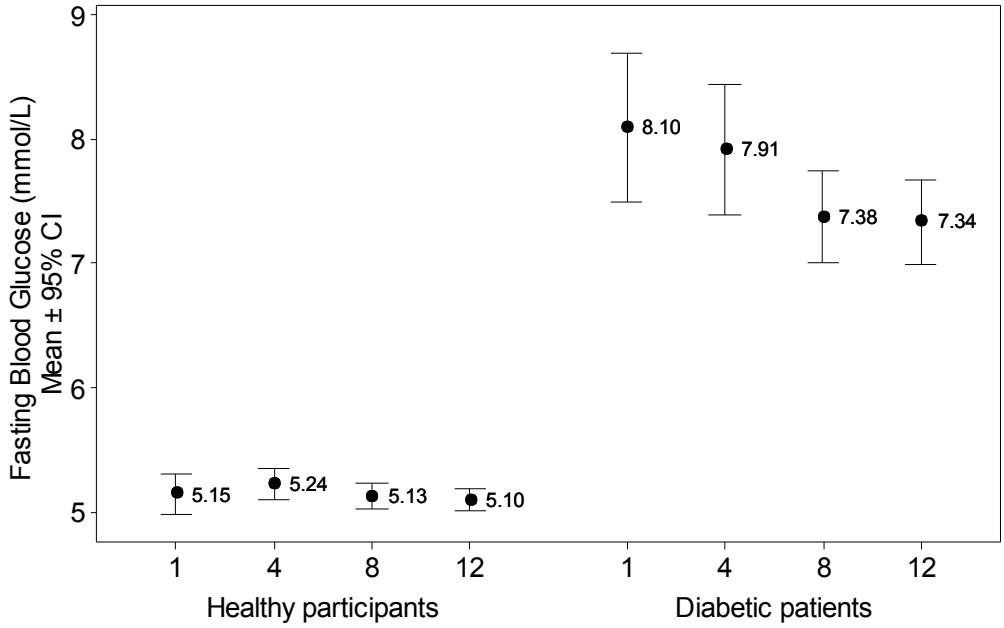

Figure 4.25. Comparison of FBG in healthy participants and diabetic patients

Table 4.12 presents the results of repeated measures ANOVA to determine the extent to which the mean FBG varied within (a) duration and the duration x health status interaction, and (b) between the healthy participants and the diabetic patients (termed the health status).

Table 4.12. Comparison of FBG in healthy participants and diabetic patients

Effect	Source of Variance	*df 1*	*df2*	*F*	*p*	Effect Size η^2
Within-subjects	Duration	3	444	13.56	<.001*	.084
	Duration x Health Status	3	432	9.21	<.001*	.059
Between-subjects	Health Status	1	148	128.41	<.001*	.465

Note: * Significant (p < .05)

The variations in FBG with duration were significant (*F* (3, 344) = 13.56, *p* < .001) with a small effect size (η^2 = .084). There was a significant duration x health status interaction (*F* (3, 342) = 9.21, p < .001) with a smaller effect size (η^2 = .059). This interaction was ordinal, because Figure 4.23 reflects that the mean levels of FBG declined with duration in both the healthy participants and the diabetics. The effect of health status was significant (*F* (1, 148) = 128.41, *p* < .001) with a moderate effect size (η^2 = .483); however, the duration x health status interaction effect indicated that the decline of FBG was most rapid among the diabetics

4.4.2.2 Two Hours Post Prandial Glucose (2hpp)

Figure 4.26 illustrates the variations in the mean levels of 2hpp ± 95% CI in the three groups of healthy participants remained below 8 mmol/L between Week 1 and Week 12, indicating that they did not have diabetes. In contrast, the mean levels of 2hpp among the diabetic patients remained above 8 mmol/L between Week 1 and Week 12, reflecting their continual diabetic condition. In the healthy participants, the mean 2hPP declined from 6.01 mmol/L in Week 1 to 6.89 mmol/L in Week 12. In the diabetic patients, the 2hpp declined from 9.53 mmol/L in Week 1 to 8.42 mmol/L in Week 12.

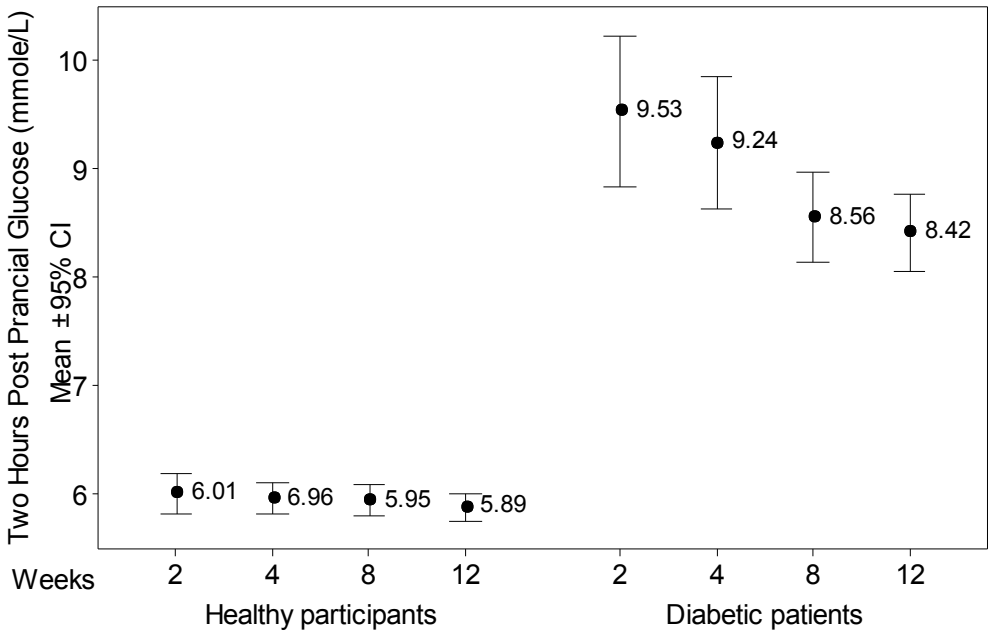

Figure 4.26. Comparison of 2hpp in healthy participants and diabetic patients

Table 4.13 presents the results of repeated measures ANOVA to determine the extent to which the mean 2hpp varied within (a) duration and the duration x health status interaction; and (b) between the diabetic and healthy participants (termed health status for the purpose of this analysis).

Table 4.13. Comparison of FBG in Healthy Participants and Diabetic Patients

Effect	Source of Variance	*df 1*	*df2*	*F*	*p*	Effect Size η^2
Within-subjects	duration	3	444	20.37	<.001*	.121
	Duration x Health Status	3	432	14.53	<.001*	.089
Between-subjects	Health Status	1	148	138.34	<.001*	.483

Note: * Significant *(p* < .05)

The variations in 2hPP with duration were significant (F (3, 444) = 20.37, *P <.001*) with a small effect size (η^2 = .121). There was a significant duration x health status interaction (*F* (3, 432) = 14.53, *p* < .001) with a smaller effect size (η^2 = .089). This interaction was ordinal, because Figure 4.24 reflects that the 2hPP levels declined with duration in both the healthy participants and the diabetic patients. The effect of health status was significant (*F* (1, 148 = 138.34, *p* < .001) with a moderate effect size (η^2 = .483). In conclusion, the decline in 2hPP indicated that the decline in 2hPP was more rapid among the diabetic patients.

4.5 Summary

- There is no significant effects of the specific dietary intake (i.e., the modified diet, the modified diet with Ajwa date, or the modified diet with *Nigella* seeds) which could be detected in the FBG levels between the three groups of diabetic patients. However, Fasting Blood Glucose levels declined between Week 1 and Week 12 in groups (D-D with modified diet and D-NS with *Nigella* seeds).
- The diets consumed by the three groups of diabetic patients (Trial 1) did not have any significant effects on the differences between the mean 2hPP glucose levels. However, Two Hour Post Prandial Glucose levels declined rapidly between Week 1 and Week 12 in groups (D-D with modified diet. and D-NS with *Nigella* seeds)
- The different dietary factors (modified diet, Ajwa and *Nigella* seeds) consumed by the three groups of diabetic patients had no significant effects on the differences between the mean levels of HbA1c of the patients. However, HbA1c levels declined significantly over duration between Week 1 and Week 12 in group D-NS (with *Nigella* seeds), the effect size was large, and there were no significant changes in HbA1c among the other two groups.
- The significant difference between the blood pressures of the three groups of diabetic patients with non-significant effect could not be interpreted because of a disordinal duration x group interaction, which meant that the effects of dietary factors on the blood pressures of the diabetic patients were inconsistent. Furthermore, Systolic Blood Pressures (SBP) and Diastolic Blood Pressures (DBP) declined over duration between Week 1 and Week 12 in group D-NS (with *Nigella* seeds). The DBP declined over duration between Week 1 and Week 12 also in group D-AJ (with Ajwa Date).
- There was no significant difference between the FBG or 2hPP levels of the three groups of healthy participants (Trial 2).
- The between- subject interaction effects with duration were the most significant outcomes of the trials. The FBG, 2hPP, HbA1c, and blood pressures declined more rapidly in diabetic patients than in healthy participants; however, the effects were only small to moderate.

Chapter 5 Discussion

5.1. Introduction

This study aimed to assess the impact of consumption of *Nigella sativa* seeds or Ajwa dates in conjunction with a defined modified diet or the modified diet alone on the Blood Glucose Levels (BGL) of diabetic patients with Type 2 diabetes and a control group of healthy volunteers. The study was divided between 2 populations. A randomised clinical trial (RCT) study was carried out in the Kingdom of Saudi Arabia and was used in the United Kingdom.

The healthy population was divided into three groups: the first group (C-D) were placed on a modified diet for 12 weeks, the second group (C-AJ) consumed the same modified diet plus 1 Ajwa date early morning (between 6am to 11am) for 12 weeks, the third group (C-NS) consumed the modified diet plus 2g/day of *Nigella sativa* seeds early morning (between 6am to 11am) for 12 weeks.

The diabetic group was focussed on adult patients with a confirmed diagnosis of Type 2 diabetes. The diabetic group was divided into three groups; each group was placed on a modified diet for 12 weeks. Group 1 acted as a control; groups 2 and 3 had their modified diet supplemented with either 1 Ajwa date (per day) or *Nigella sativa* seeds (2g/day) respectively.

The hypothesis of this study was that supplementing a basic diabetic diet with *Nigella sativa* seeds or Ajwa dates would significantly improve the control of BGL in Type 2 diabetic patients. By supplementing the diet with Ajwa dates or *Nigella sativa* seeds, there would be an increase in the nutrients and calories available and this difference may be the cause of any differences between the groups observed by the researcher.

Routine measurement of blood glucose levels is an important part of diabetes management. Hence, the BGL was measured in the early morning before any food or drink had been consumed and then again 2 hours postprandial. This was considered important as the changes in this response were taken to be an indication of differences in the response to the different diets. Moreover, the healthy groups had their BGL measured once a week, and the measurements have been used by the researcher to help with this project. The research procedure for the diabetic groups required patients to measure their BGL more than twice a week using Self-Monitoring Blood Glucose (SMBG) meters. (Chapter 3 for details of the method).

The main findings of this research is that diabetic patients who followed a dietary plan plus *Nigella sativa* seeds showed a rapid decrease of BGL (FBG and 2hPP), which was significantly greater than the control achieved in a comparable group taking only a modified diet. The findings also suggest that by using a dietary supplement of Ajwa dates, BGL remained stable throughout the 12 week period.

5.2. Trial 1 (Diabetic Subjects)

5.2.1. Demographic and Lifestyle Data

5.2.1.1. Age and Duration of Diabetes in the Diabetic groups

The demographic data shows that the diabetic participants ranged in age from 25 to 66 years. The Ajwa group, which was 40 to 66 years, was higher in age than the *Nigella sativa* and modified diet groups with the ages of participants ranging from 36- 61 and 25-62 years respectively. Previous research (AlBakr *et al.,* 2013) has reported that old age has a significant correlation with uncontrolled Type 2 diabetes. Furthermore, Memish *et al* (2014) also show that there is an increased risk of development of Type 2 diabetes in old age. This could explain why many of the diabetic participants fell within the old age category (>50 years (Karlin *et al.,* 2016). Moreover, due to the fact that there are more instances of Type 2 diabetes in women compared to men in Saudi Arabia (SA) (Memish *et al.,* 2014), this could also explain why 65% of the diabetic participants were female.

The time since initial diagnosis of the diabetic patients in the Ajwa group (D-AJ) ranged from 5 – 25 years, 1- 9 years for the group on the modified diet (D-D) and 5-10 years for the group on the modified diet plus *Nigella sativa* seeds (D-NS). Furthermore, previous research on Type 2 diabetes (e.g. Memish *et al.,* 2014) revealed that a long duration of diabetes is related to increase HbA1c levels and enhanced the risk factors related to Type 2 diabetes such as high blood pressure. Bahijri *et al,* (2016), also found that long duration of diabetes and age can lead to a rise in BGL, leading to a change in HbA1c, which supports the finding in this study that the Ajwa dates group (D-AJ) showed an increase in fasting blood glucose (FBG) and HbA1c levels in the older members of the Ajwa group (D-AJ), who had a long duration diabetes (>10 years).

As part of this study, a subgroup was extracted from each of the diabetic groups (D-D, D-AJ and D-NS) to represent the patients who had a long duration of diabetes (10 > years) and were elderly (>50 years), which was one of the factors that influenced blood glucose profile (FBG and 2hPP) and HbA1c levels (see chapter 4). One of the possible reasons for why the average in HbA1c did not decrease, could be because some of the individuals had high values of HbA1c (above 8%), FBG and 2hPP that was poorly uncontrolled. Moreover, only three out of nine patients had an improvement in HbA1c after 12 weeks of consuming Ajwa dates (see figure 4.4).However, those who were elderly and had long duration of diabetes in the *Nigella sativa* seeds group (D-NS) showed a decrease in HbA1c, FBG and 2hPP BGL levels at the end of the study compared to the baseline (the beginning of the study),

As for those patients who were elderly and had a long duration of diabetes but only consumed the modified diet alone (D-D), there was a slight increase of HbA1c, FBG and 2hPP BGL levels after 12 weeks. 2 out of the 3 patients who were from the D-D group, with a long duration of diabetes and elderly had well controlled BGL (HbA1c, FBG and 2hPP) than those from D-AJ and D-NS.
It can be seen from the graph (4.5)(see chapter 4) that the Ajwa dates seems to have an effect in diabetic people who have recently been diagnosed (short duration of diabetes < 10 years) The separation of the long duration diabetic patients (diagnosed > 10 years ago) from the short-duration diabetic patients (diagnosed < 10 years ago) reveals the difference in the effect of Ajwa dates in the two groups. Over the 12 week period of the study there is a slight fall in the HbA1c levels in the short-duration group whilst there is a rise in the HbA1c levels in the long-duration diabetes group. The division of the group into short < 10 and long > 10 years since diagnosis is essentially arbitrary hence it might be more reasonable to make the separation at another boundary such as <5> years. This has not been done as part of this study because the numbers are not considered sufficient for statistical analysis. However the theoretical justification for a differential effect of Ajwa dates is that the effect may be slight and related to insulin sensitivity/insensitivity (falling/rising) as the diabetes develops. Thus Ajwa dates have an effect in early diabetes when insulin sensitivity is still high but the effect is loss as insensitivity develops. This would also be consistent with the date flesh having low levels of an activity component

which is possibly present at higher levels in the seed also explaining why studies using ground seed or extracts of seed apparently show a greater effect. It is possible that a more detailed analysis of the data obtained in this study might assist In clarifying this but is probable that the better option would be to recommend further studies which attempt to relate activity of Ajwa to the duration of diabetes also biochemical analyses of the seed and the flesh of the date is needed to attempt to identify the specific active materials.

5.2.1.2. Smoking status

The percentage of the diabetic participants who were smokers was 33.3% (n=25), most of whom were male. Willi *et al,* (2007) concluded that the risk of diabetes is higher for heavy smokers. Moreover, Wannamethee *et al,* (2001) found that smoking could significantly increase the risk of diabetes and the complications associated with Type 2 diabetes such as failing to a healthy diet or to take adequate exercise.

The percentage of female smokers compared to male smokers from the diabetic participants was very low (n=9, 12%), which may be reflective of the Saudi culture as highlighted by the findings of Al-Nozha *et al* ,(2004).

5.2.1.3. Education Levels for Diabetic patients

The current study has shown that *Nigella sativa* seeds have the greatest effect on BGLs compared to the other two treatments. The *Nigella sativa* seeds group (D-NS) for diabetic participants had the least number of participants with a low level of education compared to the two other diabetic groups (D-AJ and D-D). 21.3% (n=16/25) of the D-NS group were identified as having a higher level of education, which is a significant point of discussion in light of earlier research. The findings of Maty *et al* ,(2005) could be used to understand why the D-NS showed a greater effect on BGL, since they highlight the observation that high education levels play an important role in positive adherence to treatment and controlling BGLs. Furthermore, Bamosa *et al,* (2007) showed that low education levels had a strong correlation with risk factors for Diabetes Mellitus. Sharaf ,(2013) and Al-Banny *et al,* (2015) came to the same conclusions, suggesting that higher levels of education may reduce relative risk factors, such as smoking, not following a dietary plan and decreased physical activity, which are more common in less educated patients . In addition, they found that a higher level of education improved the knowledge of Diabetes Mellitus and

health education for diabetic patients and found a correlation between high education levels and lifestyle modifications such as encouraging patients to follow a balanced diet (a low sugar and salt intake and increasing consumption of fruit and vegetables).

The results of this study show that 34.7% (n=26/75) of the total trial 1 group of diabetic participants were not educated beyond the primary school level. This low level of education may explain why some participants experienced difficulty in understanding their disease and how to independently follow the instructions given to them as part of the self-management programme and nutrition support plan.

Similarly, illiteracy in diabetic patients could also have had a detrimental effect on understanding the disease and that may increase the risk of complications that relate to Type 2 diabetes such as hypoglycaemia. The incidences of illiteracy in diabetic participants in all groups (D-D, D-AJ and D-NS) were low (n=9, 12%), all of whom were from the elderly female category. This could be due to the fact that elderly women in SA are less likely to be educated as historically women were socially discouraged from education (Elamin and Omair, 2010). Such participants were completely dependent on other family members keeping track of their BGL during the day.

5.2.1.4. Physical activity

As outlined in the literature review, Tuomilehto *et al* ,(2001) and Ramachandran *et al* ,(2006) found that there was a positive correlation between lifestyle modifications and diabetes prevention. Lifestyle changes such as dietary modification and increased physical activity can reduce the relative risk for the development of Type 2 diabetes.

The physical inactivity of the Saudi population is a major public health concern, especially for diabetic patients. The findings of the current study revealed that 60%, n=45/75 of all the diabetic participants were inactive, while 34% of them had up to a primary level of education (see table 4.1). This does not support the findings of Al-Nozha *et al,* (2007), who mentioned that the level of physical activity correlated with the education level of patients; those who had a lower level of education were more likely to be inactive. In addition, the findings of this study also suggest that lack of physical activity may also be due to other factors such as people's culture. Furthermore, Al-Nozha *et al,* (2007) also found that

females were less physically active than males. This could be due to the fact that there are a limited number of environments in which females can be physically active (such as health centres or gymnasiums), and any such facilities that do exist are expensive.

Moreover, most of the elderly diabetic participants of this study had low levels of physical activity. The researcher's information gathered at the initial meetings with such participants imply that this could be because of the hot weather conditions in SA, which makes it difficult for them to be physically active outdoors during the day. Another possible explanation for this trend could be the inability of elderly people to exercise frequently due to other health conditions.

5.2.1.5. Body Mass Index (BMI)

The results of the present study show that the BMI of all the participants ranged from 18 to 47kg/m^2, with the average being 26.8kg/m^2. Despite patients being randomly assigned to the different group which should have ensured that pre-existing factors did not influence the study it can be seen that the BMI of the Ajwa group is different.

Memish *et al*, (2014) and Al-Daghri *et al,* (2011), found that an increase in BMI leads to an increase in HbA1c levels and a BMI of more than 26 – 30 may increase the risk factors of Type 2 diabetes. Consistent with the findings of Memish *et al,* (2014) and Bahijri *et al,* (2016), this study found that the participants with a higher BMI in D-AJ group had higher levels of HbA1c.

This study showed that the BMI for the 2 diabetic participant groups following the specific supplementary diets assigned to each group (*Nigella sativa* seeds and Ajwa dates), declined after 12 weeks. This supports the findings of Hoseini *et al,* (2013) who concluded that *Nigella sativa* intake produced a significant reduction on BMI. However, there are numerous studies illustrating that *Nigella sativa* has a non-significant effect on BMI. (Qidwai *et al.,* 2009; Haque *et al.,* 2011 and Shah *et al.,* 2012).

The contradictory findings of other studies may be reflective of the fact that they each used a different dosage of *Nigella sativa* and were carried out over different duration. For example, Qidwai *et al,* (2009) used 1g/day for six weeks, whereas Haque *et al,* (2011) used 5ml of *Nigella sativa* oil/day for six weeks and Shah *et al*., 2012) used 500mg/day for the same duration. Although Hoseini

et al's (2013) study used the same dosage of *Nigella sativa* as Haque *et al,* (2011), their study (ibid, 2013) was carried out over a period twice as long as Haque *et al*'s (2011).

All the studies which concluded that the BMI reduction was insignificant as a result of using *Nigella sativa* were carried out over a period of six weeks. Whereas the studies, including this one, which were carried out over a longer duration (12 weeks), found a significant reduction in BMI. Therefore, it is important to consider the differences in the dosages of *Nigella sativa* used *as well as* the duration of each of the studies. One of the reasons why the findings of Hoseini *et a,l* (2013) are consistent with the findings of this present study could be because both these studies allowed 12 weeks of *Nigella sativa* intake in order for a significant reduction in BMI to be observed.

5.2.1.6. Measuring Blood glucose level SMBG

Many research studies (Rubin *et al.*, 1989; Hirsch *et al.*, 2008; Durán *et al.*, 2010) have concluded that self-monitoring blood glucose is one of the most effective ways of self-managing type 2 diabetes. This is because it allows the patient to be aware of their own BGL, giving them the opportunity to change their behaviour, resulting in better control of the BGL through dietary restraint. The fact that 60% of the diabetic participants of this study, did not do the Self-Monitoring Blood Glucose measurements at home is reflective of the findings of Huri et al, (2010), who found that patients preferred to do the measurements at the hospital, as it was easier for them to have a health professional, such as a nurse, do the measurements for them; despite having all the tools to measure BGL at home. The possible reasons for this could have been a fear of pain associated with the tests and difficulties in reading the results, especially for the illiterate participants.

As demonstrated in chapter 4, there was a fluctuation in the BGL (FBG and 2HPP) of all three diabetic groups over the 12 week period. Among the reasons for this could be due to 60% of participants taking their BGL measurements at the hospital rather than at home. Therefore, the frequency of monitoring their BGL was dependent on the frequency of their hospital appointments, which in some cases were monthly.

Summary

In summary, it is important to consider the demographic and lifestyle data discussed above when analysing the results of this study because it is possible that this data may influence the BGL and blood pressure. It would appear that the level of education is a key factor for people in SA, including those with diabetes, in influencing their lifestyle choices. This is because there is a strong positive correlation between low levels of education and lifestyle modifications such as reducing smoking, increasing physical activity and frequently measuring BGL in order to be able to manage the disease.

5.2.2. Discussion of individual parameters in the Diabetic group

5.2.2.1. Fasting Blood Glucose Levels (FBG)

The results in the present study suggest that the FBG level for trial 1 (diabetic group) D-NS and D-D groups declined over the 12 weeks of the study. However, the FBG level of the D-AJ group remained constant over the 12 weeks of the study. Over the duration of this study, the researcher observed that time had a significant effect on the FBG level, with P (<0.001), within the diabetic groups. The data shows that the Ajwa date group (D-AJ) started with a significantly lower mean FBG than the other 2 groups and that the levels in these 2 groups (D-D and D-NS) falls only into the range in which the Ajwa date group remain, suggesting that the FBG in the Ajwa group was already under control. The possible explanation for the fact that the BMI appears to be reduced more in the Ajwa group and the diet group. (Figure 4.1) is that the Nigella seeds provide some additional nutrition.

In the present study, a reduction in FBG was observed in Type 2 diabetes patients, who had a diet supplemented with 2g of *Nigella sativa* seeds (D-NS). This supports the findings of Bamosa *et al*, (1997), who studied the effect of different doses of *Nigella sativa* seeds on blood glucose in healthy volunteers in SA. They (ibid, 1997) found that 2g of *Nigella sativa* seeds resulted in a significant decrease (P<0.05) in FBG after inclusion in the diet for 2 weeks. The findings of this study are also consistent with previous research on patients with Type 2 diabetes, (Bilal *et al.*, 2009; Bamosa *et al.,* 2010; Ahmed *et al.,* 2012; Najmi et al., 2012 and Hoseini. *et al.,* 2013) all of which show a significant effect of *Nigella sativa* on FBG. Furthermore, Bamosa *et al* ,(2010) found that 1g of

Nigella sativa seeds had no significant effect on FBG levels over a 3-month period, which was in contradiction to the findings of Ibrahim et al (2014), who used the same dose of *Nigella sativa* seeds, and found a significant effect on FBG over a 2-month period. One of the reasons for the inconsistency in their results could be due to the fact that the participants used for each of the above mentioned studies, had an impact on the overall result. When comparing these studies, it is essential to consider the fact that Ibrahim *et al,* (2014) only studied the effect of *Nigella sativa* seeds on menopausal women aged 50-55, whereas Bamosa *et al,* (2010) studied males and females aged between 18-60.
Based on the previous research (outlined in chapter 2) on *Nigella sativa* seeds and their effect on FGB, there does not appear to be a consistent trend in the amount of *Nigella sativa* seeds given and the effect on FBG. For example, Datau *et al's* (2010) result of a non-significant change in FBG ($p>0.05$) leads to further speculation. This may be because their study was based on obese men but it was not clear as to whether or not they also had Type 2 diabetes, hence it may or may not be comparable with other studies in diabetic patients. Therefore, the duration of studies, the dose of *Nigella sativa* used, and the status of participants are all essential factors to be considered when comparing studies.

There is a lack of studies that observe the effect of Ajwa dates on FBG levels in humans. Despite the report of Hasan and Mohieldein (2016), who found that there was a significant decrease in FBG in diabetic rats when given 10 ml of Ajwa date seed extract, this is not a justification for adding Ajwa dates to the diet. The reason being that they used an extract of Ajwa date seeds which clearly is significantly different biochemically from the flesh of the date hence the properties are significantly different. Care should be taken when examining pervious study because of variation in the materials actually used. References show that rather than the flesh of the date many studies used the seeds either ground or as an extract and of course with different method of extraction being used, all of which results in different material which produce different results.

5.2.2.2. Blood Glucose Levels (2hPP)

Over the 12 weeks of the present study, there were significant changes ($P<.001$) in the 2 hour postprandial BGL of all diabetic groups. The statistical difference (see chapter 4, figure 4.2) shows a clear fall in both parameters from

a mean of 9.96 mmol/L in week 1 for D-D to a mean of 8.70 mmol/L in week 12, and from a mean of 10.25 mmol/L in week 1 for D-NS to a mean of 8.29 mmol/L in week 12. In contrast, the group consuming the modified diet supplemented with Ajwa dates (D-AJ) did not show a fall over the study period but unexpectedly this group started the study with a value of 8.39 and although there was variation, week 4 = 8.50, week 8 = 8.23 and week 12 = 8.29, remained constant throughout the study.

The D-AJ group coincidently had low values for FBG and HbA1c at the beginning of the study, which resulted in the average 2hPP BGL of the D-AJ group being already as low as the other 2 groups became (D-D and D-NS). Although it is possible to interpret this difference in figures as being a result of selecting participants for the Ajwa group, rather than randomly assigning them, the study design (outlined in chapter 3) clearly shows that this was not the case, as patients were assigned to each of the groups (D-D, D-AJ and D-AJ) depending on their time of arrival to the diabetes clinic, at different days throughout the period of collecting diabetic participants. One possible reason for the significant difference in the baseline readings, could be due to the unbalanced nature of the groups due to being randomly assigned to each of the three groups. Thus, the significant fall in 2hPP BGL in the D-D and D-NS groups only brought their values down to the level of the D-AJ group.

Previous research (e.g. Rahman, 2007; Bandeira *et al.,* 2012 and Hasan and Mohieldein, 2016) suggests that the presence of flavonoids and antioxidants in the Ajwa date could reduce the oxidative stress by an antioxidant enzyme, leading to a reduction in BGL. However, this was not the case from the results of this study. Thus care should be taken when considering these results, as after 8 weeks and 12 weeks the results appear to show a fall in both these parameters when compared to the week 1 and week 4 data (figures 4.2 in chapter 4), suggesting that this fall could be an anomaly. Furthermore, this could also be because the basic results show that the D-AJ group had mean values, which appear to be lower than the mean values on all data of the other 2 groups (see 2hpp figure 4.2 for trial 1). One possible reason for no reduction in BGL for the Ajwa group, could be due to the reduction of most polyphenols (natural antioxidants) at the tamar stage of the growth of dates (details mentioned in chapter 2)

In addition, the significant fall in 2hPP BGL for the D-NS found in this study also support the earlier study of Bamosa *et al,* (2010), who showed that 2hPP blood glucose level were affected by treatment with *Nigella sativa* seeds. Also in support of the above results, Najmi *et al,* (2012) demonstrated that *Nigella sativa* with 500 mg a day for 8 weeks had a significant effect on the 2hPP blood glucose in diabetic patients.

5.2.2.3. Glycated Haemoglobin HbA1c

The current study found a reduction in HbA1c levels in the D-NS group with a dose of 2g per day of *Nigella sativa* seeds after 12 weeks compared to the baseline (the starting value). These findings are consistent with many previous studies (Bamosa *et al.*, 2010; Mohtashami *et al.*, 2011; Najmi *et al.*, 2012 and Hoseini *et al.*, 2013), which found that *Nigella sativa* ingestion is associated with improvements in the HbA1c levels and that a *Nigella sativa* supplement could have a positive impact on patients with Type 2 diabetes, dependent on the doses and duration of treatment. According to Bamosa *et al*'s (2010) clinical trial analysis of 68 Type 2 diabetes patients, a study duration of 12 weeks taking a dose of 2g/day produced a significant reduction in HbA1c levels. They (ibid, 2010) suggest that the effect of *Nigella sativa* seeds on the levels of insulin resistance may improve the function of B-cells leading to a reduction in HbA1c. In contrast, patients who followed a modified diet (D-D) or a supplemented modified diet with an Ajwa date (D-AJ), showed no significant change in HbA1c levels. Research on the Ajwa date is very limited and there is a lack of studies carried out on humans to test the effectiveness of the Ajwa date flesh and their effect. Thus, this study aimed to address this gap in research by using the Ajwa date flesh as a supplement to the modified diet for one of the control groups (D-AJ).

However, studies have been carried out to test the effect of Ajwa date seeds (e.g. Khalid *et al.,* 2016) and their extracts (e.g. Baliga *et al.,* 2011). Another such study was that of Hasan and Mohieldein (2016), who tested the effects of Ajwa date seeds extract on diabetic rats and demonstrated a significant decrease in blood glucose levels after 8 weeks at a dosage of 10 ml/day. The treatment also produced a significant decrease in the rats' HbA1c levels as well as producing enhanced insulin levels and improving glycaemic control.

The part of the Ajwa date used in each of these studies is vital to consider. A possible explanation for the positive effects of the Ajwa date seed extract could be due to the presence of flavonoids and phytoconstituents, which could be the reason why Ajwa dates seeds had an anti-diabetic activity(Kalantaripour *et al,*(2012) and Said *et al,* (2014). Therefore, although the findings of this study show that there was no significant change in HbA1c levels for D-AJ, this could have been anticipated, since it could be seen to be in agreement with the conclusions of previous research, which found a positive effect of the date seed/extract rather than the flesh. The findings of Khalid *et al,* (2016) also highlight that Ajwa date seeds contain more proteins, crude fat and crude fibre when compared to the flesh.

Summary

In summary, when comparing all three diabetic groups, the D-NS group showed the most change in FBG and 2hPP. This could be because treatment with *Nigella sativa* may cause a reduction in gluconeogenesis in the liver, which leads to a decrease in FBG (Fararh *et al*, 2004). Moreover, a possible reason for the reduction in the FBG level and HbA1c in patients consuming *Nigella sativa* is that it may cause an inhibition in the intestinal absorption of glucose and this may lead to an improvement in glucose tolerance (Meddah *et al*, 2009). In addition, according to Alsaif (2008) and Abdelmeguid *et al,* (2010), *Nigella sativa* also has a beneficial effect on pancreatic B-cells as it causes an increase in blood insulin levels and lowers blood glucose levels.

Furthermore, Ajwa dates seeds had more polyphenols (as form of antioxidants) than Ajwa date flesh (Khalid *et al.,* 2016), which cause a decrease in oxidative stress, leading to a decline in FBG and HbA1c. Despite this fact, the FBG and the 2hPP levels of the D-AJ group remained constant. This could be due to the lack of adherence of participants to the recommended diet or not having an Ajwa on a daily basis. The limited amount of research on the effect of Ajwa dates on diabetes makes it difficult to speculate further on the reasons for this finding.

Furthermore, another explanation for why the results of the D-AJ were significantly different from the other groups could have been due to the lack of compliance to modified the diet, and the participants in D-AJ not following the dietary intake of an Ajwa date daily. It can be difficult for the researcher to follow and understand the compliance of the participants throughout the study.

5.2.2.4.Blood Pressure (Diastolic and Systolic Blood Pressure)

One of the major risk factors for Type 2 diabetes is hypertension, for this reason the participants' blood pressures were measured on a weekly basis for the 12 weeks of the study. There was a rapid fall in systolic blood pressure (SBP) between week 1 and week 12 for the *Nigella sativa* seeds diet group (D-NS). There was an initial fall in SBP from week one and week four results for both D-D and D-AJ. These results changed significantly for all 3 groups over the 12 week study period with P<.004. A possible reason for why this occurs could be as a result of the change from normal to the modified diet, but may have been masked by nutrients in the 2 supplements, or due to lack of compliance to the diet. Furthermore, the D-D results for weeks 4,8 and 12 show a gradual rise, which possibly show that the initial change to a modified diet was good but that there was a gradual loss of effect or possibly due to the patients are not "sticking" to the diet.

In contrast the Ajwa group showed a smaller fall but there was no subsequent rise.

Interestingly the average diastolic blood pressure (DBP) rapidly declined in two groups, the D-AJ and D-NS, from week one (83 and 87) until week 12 (77 and 79) respectively. However, there was a slight initial decline from week one (82) to week four (81) but then the average DBP for the modified group (D-D) started to rise in week 8(82) and fall again in week 12 (81) and did not change significantly. A possible reason for that could be because the modified diet had less effect on DBP. Moreover, those who consumed the modified diet plus Ajwa and *Nigella sativa* seeds showed a greater effect on DBP than those who only followed the modified diet alone.

These findings support earlier studies that found a relationship between dietary intake of *Nigella sativa* seeds and reduction of blood pressure (SBP and DBP) (Dehkordi and Kamkhah, 2008; Elrehany *et al.*, 2012; Fallah Hoseini *et al.*, 2013 and Najmi *et al.*, 2013). Dehkordi and Kamkhah, (2008) randomly split 108 patients suffering from mild hypertension, into 3 groups, using a double blinded clinical trial with 200 mg and 400 mg daily of *Nigella sativa* extract for 8 weeks. Despite the use of an extract of *Nigella sativa* seeds from northern Iran, and a difference in dose and duration to this study, they (ibid, 2008) also found that the intake of *Nigella sativa* extract had a significant decrease on blood pressure ($P < 0.05$).

More recent studies also support the positive effect of *Nigella sativa* on blood pressure. A clinical trial in Egypt by Elrehany *et al,* (2012) recruited 55 patients with coronary artery disease and dyslipidemia, who they treated with a dose of 900 mg of Ns seeds daily for 8 weeks and found that there was a significant change in blood pressure (P <0.001). Furthermore, Najmi *et al,* (2013) suggest that the use of *Nigella sativa* seeds in patients with metabolic syndrome had a positive impact on blood pressure and concluded that following administration of NS seeds for 8 weeks at a dose of 500 mg daily, there was a highly significant decline (P<0.001) in blood pressure. Despite the use of NS oil, the findings of Fallah Hoseini *et al,* (2013) are in agreement with the conclusions of Elrehany *et al*'s (2012) study. They (ibid, 2013) reported on the effect of NS oil on the blood pressure of healthy subjects in Iran, with 5 ml daily for 8 weeks, and showed a significant decrease in both systolic and diastolic blood pressure
Elrehany *et al,* (2012) and Najmi *et al,* (2013) both used a dose of *Nigella sativa* seeds, 900 mg and 500 mg respectively, but Fallah Hoseini *et al,* (2013) used 5 ml of the oil. When comparing studies that used seeds and oil, it is important to discuss key differences between these substances, which may have an effect. Firstly, oil is an extract from the whole seed so it will take more than 5g possibly 10 or more grams of seed depending on the percentage oil which can be extracted. Secondly, the difference in chemical composition between the oil and the whole seed could suggest that the active ingredient is not oil soluble and in fact exists in higher concentrations in the pulp left following oil extraction. Many researchers (for example El Tahir *et al.*, 1993; Al Tahir and Ageel, 1994; Dogan *et al.*, 2010 and Fallah Hoseini *et al.*, 2013) suggest that the reason for the reduction in blood pressure in patients using *Nigella sativa* seeds, as part of a modified diet, is that the seeds contain anti-oxidants in the form of unsaturated fatty acids, such as oleic and linoleic acids and polyphenols (Mahmmoud and Christensen ,2011)

Miura *et al,* (2008) conducted an international cross-sectional epidemiological study of 4680 males and females aged between 40 and 59 years, and compared the effects of macro and micronutrients on blood pressure. They conducted a 24 hour dietary recall for each person and found that linoleic acid was one of the main dietary polyunsaturated fatty acids (PUFA). Their

conclusions support the theory that including linoleic acids intake in a dietary plan may have a beneficial effect on controlling blood pressure.

Among the reasons presented in the literature, for the lowering of blood pressure, are that *Nigella sativa* is a rich source of polyphenols and flavonoids, which have antioxidant activity, particularly thymoquinone, and also has free radical scavenging properties (Khattab and Nagi, 2007; Fallah Hoseini *et al.,* 2013). Another possible explanation for the improvement in blood pressure measurements, from studies using *Nigella sativa* oil, could be that the volatile oil present in *Nigella sativa* oil may cause a decrease in arterial pressure (El Tahir and Ageel, 1994). Based on previous studies by Khattab and Nagi (2007) and Fallah Hoseini *et al,* (2013) the findings of this study suggest that the reduction in blood pressure is due to *Nigella sativa* seeds being a rich source of antioxidant such as thymoquinone.

Interestingly, the correlation between a decline in blood pressure and *Nigella sativa* seeds intake is reported to be related to a decreased angiotensin-converting enzyme activity (Mohtashami and Entezari, 2016). In addition, Andriambeloson *et al,* (1998) and Khattab and Nagi (2007) reported that *Nigella sativa* is rich in flavonoids, which lead to an increase in nitric oxide, causing a fall in blood pressure. Furthermore, Jaarin *et al,* (2015) claim that treatments using *Nigella sativa* seeds may have an anti-hypertension effect on patients due to lowering of cardiac oxidative stress.

On the other hand, there are several studies that found that there was no improvement in blood pressure using *Nigella sativa* (Najmi *et al.*, 2007; Qidwai *et al.*, 2009; Datau *et al.*, 2010; Shah *et al.*, 2012 and Ibrahim *et al.*, 2014). A randomised clinical trial study by Najmi *et al,* (2007) of 161 metabolic syndrome patients given a daily dose of 5 ml of *Nigella sativa* oil for 6 weeks, found that there was no significant change in blood pressure. This could be because when comparing 5 ml of NsO with 2g of *Nigella sativa* raw seed it is important to note that the 5ml of oil is likely to have less effect than 2g of raw seeds. The reason for this can be explained as a result of the dose ratios between oils and the actual seed. If the density of the oil is assumed to be 1.0 then 5 ml is equivalent to 5g of seed if the yield of oil is 100% (i.e. the density of the oil is the same as the seeds). More realistically, the yield of oil from seed is approximately 30% (Gholinezhad and Abdolrahimi, 2014), thus 5ml of oil is equivalent to approximately 16g of whole seed, which suggests that as 2g of seed works, that

the oil is far less effective. A dose of approximately 16g would make the dose used in Najmi et al, (2007)'s study 250% higher than the dose used in this study, making it above the range of *Nigella sativa* that is recorded to be effective (as mentioned in chapter 2).

Furthermore, Qidwai *et al,* (2009) conducted a study for the same duraion (6 weeks) with 73 adults in Pakistan, who were randomly given 1g of *Nigella sativa* seeds daily. Despite the fact that Najmi *et al,* (2007) used 2.5 ml of *Nigella sativa* oil twice a day and Qidwai *et al,* (2009) used seeds, both found that there was no significant effect (P>0.05) on blood pressure over the same duration.

It was later shown by Datau *et al,* (2010), that even at a longer duration, *Nigella sativa* seeds at a dose of 1.5 g/day did not reduce blood pressure. Datau *et al* ,(2010) conducted a double blinded, randomised control trial on 39 obese men, to whom *Nigella sativa* seeds were given daily, for 3 months. At 3 months, the blood pressure levels were not significantly improved (p>0.05). Two years later, a similar study was done by Shah *et al,* (2012), whereby a clinical trial was conducted of 159 metabolic syndrome patients given 500 mg daily of *Nigella sativa* seeds for 6 weeks, and there was no significant difference in blood pressure. This is also consistent with the findings from another study involving 37 randomly selected menopausal women (aged 50-55), who followed a diet including 1g of *Nigella sativa* seeds powder per day for 2 months (Ibrahim.R.M *et al*., 2014).

The findings of this study contradict the findings of the above mentioned studies. Among the reasons for this could be the fact that none of the above studies that looked at the effect of *Nigella sativa* on blood pressure, used Type 2 diabetes participants. This is a very important factor to consider as one of the complications related to patients with Type 2 diabetes is hypertension. Therefore, any changes in BP would be more clearly observable in patients with Type 2 diabetes.

Furthermore, another possible reason for the non-significant change in BP found in the previous studies, could have been because of the different doses of *Nigella sativa* used. This study used a dose of 2g/day of raw *Nigella sativa* seeds, which was higher than any of the doses used in the above mentioned studies. Therefore, the dose of *Nigella sativa*, may have an impact on the change in the BP.

In addition, another possible reason for the non-significant change observed in previous research could also be due the fact that in all of the previous studies, *Nigella sativa* was just added to the normal diet of participants rather than a modified diet. The findings of this study may differ from the results of previous research due to the fact that participants were instructed to follow a modified diet (for details see chapter 3) and the adherence to the modified diet of the D-NS group was high. Therefore, the decline in BP may reflect the effect of the *Nigella sativa* seeds more accurately over the 12 weeks of the study. The findings of this study suggest that the use of a modified group alone (D-D) could cause a change in SBP. However, it would appear that the use of *Nigella sativa* seeds as a supplement to a modified diet had a greater impact on SBP when compared to just a modified diet alone.

The DBP on the D-AJ group also decreased significantly. One of the reasons for this could be because Khalid *et al,* (2016) noted that Ajwa also contain antioxidant activity, polyphenols, flavonoids and antiviral activities. Khan *et al,* (2014) found that Ajwa dates have a phenolic component of 7.3 mg/kg and free radical scavenging activities, which could cause a fall in blood pressure in people who consume Ajwa dates.

Khalid *et al,* (2016) also reported that Ajwa date flesh have a higher amount of potassium (4.8 mg/100 g) than Ajwa date seeds (4.7 mg/100 g). This is significant because most of the studies on Ajwa have used the seed or extract from the seed, whereas this study used the flesh of the Ajwa. Therefore, it is not surprising that the DBP for the D-AJ decreased significantly as this could be due to the higher level of potassium in the flesh when compared to the seed.

In addition, Assirey (2015) reported that the Ajwa date is a rich source of potassium. Ajwa dates contain less sodium than potassium making the balance beneficial, which could be the reason for the improvement in blood pressure level of hypertension patients. Chang et al. 2006 reported that the balance of sodium/potassium (1/16) ratio is a very important aspect of a healthy diet, as well as a reduction in the salt intake, which should be less than (6 g/day) (Assirey, 2015). Du et al. 2014 claims that a balance of sodium and potassium intake is nutritional and health-wise the best option. They (ibid, 2014) state that this balance can be reached by adding high potassium foods to one's diet (such as white beans, sweet potato, winter squash, milk, avocado, spinach and salmon).

The SBP remained consistently low in the Ajwa group (D-AJ), but there was no significant decrease in the SBP. A possible explanation for this, could be due to the different types of antioxidants activity present in Ajwa date flesh compared to *Nigella sativa* seeds. Another possible explanation could be due to the difference in concentration of antioxidant activity in Ajwa and *Nigella sativa*. If Ajwa dates have less antioxidant activity then it may explain why they have no significant effect on SBP.

Moreover, the reduction in SBP for diabetic patients could be due to the decrease in BMI after consuming Ajwa dates for 12 weeks (see chapter 4, figures (4.3 and 4.4).

Summary

The present study illustrates a significant improvement in the blood pressure of diabetic patients ($p<0.05$) in the *Nigella sativa* seeds 2g/day group (D-NS). In contrast only the DBP falls in those patients consuming Ajwa dates (D-AJ). However, there was no significant decline in the SBP and DBP in participants on the modified diet regime, indicating that the effects observed were due to the dietary supplements. Thus there might be significant nutritional advantages in including both these supplements in a modified diet.

5.3. Trial 2 (Healthy Subjects)

5.3.1 Demographic and Lifestyle Data

The demographic data illustrates that the healthy participants ranged in age from 20 to 60 years. Generally, the results of trial 2 show that the BMI of all healthy participants ranged from 18.61kg/m^2 to 37.02 kg/m^2 (with the average being 25.53 kg/m^2) and that most of the healthy subjects were overweight. (Malik *et al.*, 2013 and Memish *et al*, 2014), reported that an increase in BMI leads to an increased risk of obesity and a BMI of over 30 could increase the risk factors associated with type 2 diabetes. Despite the BMI level being higher in the *Nigella sativa* group (C-NS) when compared to the modified diet group (C-D), there was still a reduction in the FBG in the C-NS.

There is a reduction in the BMI level at the baseline for the whole trial 2 group, after following the modified diet over the 12 weeks. However, the *Nigella sativa* group had the same modified diet plus 2g/day of *Ns* and showed a decrease in FBG over the 12 weeks.

In trial 2, there was a reduction in weight for all healthy participants compared to the measurements at the baseline (See figure 4.18). Datau *et al,* (2010) mentioned that *Nigella sativa* (1.5 g daily for 3 months) caused a significant ($P<0.001$) reduction in body weight in obese men aged from 30 to 45 years. Similarly, Ibrahim *et al,* (2014), also reported that a dose of 500 mg of *Nigella sativa* seeds powder daily for 8 weeks, in women aged from 45 to 60, caused a slight decrease in the body weight but it was not statistically significant. However when the 8 weeks of dietary intake of *Nigella sativa* seeds powder was over, there was a dramatic increase in body weight (ibid, 2014). Moreover, Dehkordi and Kamkhah (2008) reported that there was no significant decline in body weight after treatment with *Nigella sativa* seeds extract with 100 mg and 200 mg daily for 8 weeks.

Previous research (Memish *et al.*,2014) has reported that a high BMI (being obese) has a significant correlation with incidences of Type 2 diabetes. Furthermore, Chen *et al,* (2013) also show that there is an increased risk of CVD in people with a BMI within the obese range. At the baseline 13% of the healthy volunteers were obese with a BMI > 30 kg/m^2, after 12 weeks of following a specific diet, the percentage of healthy subjects that fell within the obese range fell to 11% (see figure 4.19). However, 11% from the healthy

subjects need to manage their weight as they are at risk of developing type 2 diabetes.

Most of the healthy participants had a high level of education (72%), which was most likely due to the fact that healthy participants were recruited within close proximity to a university. This could explain why 77.3% of the healthy participants were active. Bassuk and Manson (2005), reported that being active could reduce the risk of having type 2 diabetes and cardiovascular disease.

Sharaf (2013), found that a high level of education (university level) leads to an increase in awareness of physical activity. Midhet *et al,* (2010) reported that the level of high school education or lower of Saudi's, leads to physical inactivity and an unhealthy dietary intake. However, the Saudi's who had a high level of education (undergraduate and postgraduate) demonstrated a healthy dietary intake and were physically active Midhet *et al*., 2010.

Within the trial 2 group, the BMI for the C-D appeared to decline after 12 weeks compared to the other 2 groups. This may be due to additional nutrients provided by supplement which obscured the fall in BMI which might have occurred.

All of the healthy participants had good BMI which is probably the results of physical activity. This supports the findings of Hawley (2004) and Fareed *et al,* (2017) who concluded that being active had a significant effect on BMI. Previous studies (Hodge *et al.*, 2004 and Mohan *et al.,* 2009) have also mentioned that following a dietary plan including wholegrain, fibre and a reduced intake of red meat is associated with a decreased risk of type 2 diabetes. Furthermore, Muraki *et al,* (2013) also reported a relationship between a dietary intake of whole fruit, such as apple, blueberry and grapes and a decreased risk of type 2 diabetes.

5.3.2 Discussion of individual parameters in healthy groups

5.3.2.1 Blood Glucose Levels (FBG and 2hPP)

There was an observable decrease in the FBG levels of the healthy participants, who followed the modified diet supplemented with 2g/day of *Nigella sativa* seeds (C-NS). This result supports the findings of a previous study by Bamosa *et al*, (1997), who examined the effect of 2g/day of *Nigella sativa* seeds on adults for 2 weeks and found a significant decline in FBG levels. This could be due to the mechanisms by which NS has its effect on the reduction of BGL as mentioned in the trial 1 (diabetic group) section. Furthermore, Mohtashami *et al,* (2011) mentioned that using a dose of *Nigella Sativa* oil (5ml) daily for 2 months had a significant P(<0.05) effect on the FBG of healthy adults.

However, in-group C-D, following only the modified dietary plan, and C-AJ, following the modified diet with an Ajwa date, a non-significant fluctuation was observed in glucose levels (fasting blood glucose, FBG) in healthy participants after 12 weeks. This could imply that the Ajwa dates do not have an effect on the FBG levels of healthy people. Moreover, another possible explanation for this finding may be a lack of adherence to the treatment or diet.

The C-AJ results began significantly lower than the other 2 groups. The C-NS group values fell significantly but the end point was remarkably close to the values of the C-AJ group suggesting that the C-AJ was selected specifically rather than the volunteers being randomly assigned and that the AJ group were the healthy group with specific advantages compared to the other groups. Also the modified diet group showed no reduction in values but this group is also higher than any value observed in the other groups. Although there was a significant difference (P<.001) in the 2hPP blood glucose levels, between all the healthy groups, the *Nigella sativa* seeds group (C-NS) showed a rapid decrease in 2hPP but the modified diet (C-D) and Ajwa date (C-AJ) groups did not have a noticeable decrease in the 2hPP BGL. As discussed earlier in trial 1, this could be due to the active component (Thymoquinone), found in NS, which could reduce the BGL.

5.4.Trial 1 and Trial 2

In this study, both the diabetic group (Trial 1) and the healthy group (Trial 2) had a fall in fasting blood glucose (FBG) from week 1 (8.10 and 5.5 mmol/L) to week 12 (7.34 and 5.1 mmol/L) respectively, with a significant decrease within both trial groups over the 12 weeks (P <.001). Furthermore, the difference in the mean of the 2hPP levels in the 3 groups of healthy participants was below 8 mmol/L and the variation in the mean of the 2hPP levels in the 3 diabetic groups was above 8 mmol/L. This simply due to the fact that the healthy group already had a low value and hence any fall would probably be small i.e. as observed. 0.4mmol/L, whereas the diabetic groups began with an unhealthy high value which made it possible to have a large fall from the unhealthy high value to a normal value. However the fall is only to 7.34mmol/L which is still high but it is a fall of 0.8mmol/L. So in both cases the fall is approximately 10% of the original value which may allow the statement that the fall in 2hPP is equivalent in both groups.

There was a significant decline in 2hPP levels over the 12 weeks within both trial 1 and trial 2 groups (P <.001). One possible reason for why there were different results in the FBG and 2hPP BGL could be due to the different places of recruitment (the trial 1 group was recruited in SA and the trial 2 group from the UK). It is expected that the healthy participants (Trial 2) being more active and having a lower BMI than the diabetic group (Trial 1), and therefore the results for the diabetic group should be more significant than those seen in the healthy group. It is important that being physically active and following a modified diet is more effective than following a modified diet alone.

Summary

Generally, the healthy groups in trial 2 had a high level of education and physical activity that lead to a decrease in the BMI after 12 weeks of specific dietary intake. The *Nigella sativa* group for the healthy participants (C-NS) had a fall in FBG and 2hPP from week 1 to week 12. However, the modified diet alone (C-D) appeared to produce a statistically non-significant reduction in both parameters, FBG and 2hPP blood glucose levels, whilst the modified diet plus Ajwa dates (C-AJ) started and finished at a level which did not change and was equal to the final value compared to the other 2 groups in this trial whose values fell but began higher than those of the Ajwa group and only fell to a level equivalent to the level of the Ajwa group. Suggests that the Ajwa date group were at the lowest achievable level throughout the study whilst the other two cohorts were initially abnormal and improved.

There was a significant difference between the 2hPP levels of the three (C-D, C-AJ and C-NS) groups ($p < .001$).The reason for this is not understood and need further examination.

Overall, it is clear from this study that the consumption of a supplemented of modified diet reduced FBG and 2hPP.Clearly the diabetic groups had significantly higher mean values of BGL than the healthy groups, which is in line with expectation, but although the diabetic group of volunteers were randomly assigned to the three test diets, it is clear that the means at week one are different between them 3 diet groups. Despite this, there was a significant decreased in FBG and 2hPP BGL in diabetic patients (trial 1) when compared with the healthy participants (trial 2).

5.5. General Discussion

The aim of this study was to investigate whether a modified diet supplemented with either *Nigella sativa* seeds or Ajwa dates had an effect on markers of diabetic control.

Recent research (Memish *et al.*, 2014) has revealed that Saudi Arabia is one of the countries in the middle east with the highest incidences of Type 2 diabetes. As a result of the current global Type 2 diabetes epidemic, there is great interest in the contribution of dietary factors to the prevention of this disease. Some studies have shown that a plant based diet has proactive effects against the development of metabolic complications such as insulin resistance. These beneficial effects have been related to the presence of polyphenolic compounds, which possess a wide range of biological properties including antioxidant and insulin sensitizing activities. Additionally, growing evidence has demonstrated that diets rich in polyphenolic compounds may also regulate and improve glucose and lipid metabolism. Accordingly, diet modification programmes can be employed as an alternative approach to control the risk of Type 2 diabetes (Jung *et al.*, 2006). In order to reduce the high prevalence of T2DM in SA, Albakr *et al,* (2013) proposed that diabetes clinics around the country should encourage patients to practice self-management and provide practical training for those who are poorly educated or illiterate. For example, providing the appropriate skills that help them to improve the glycaemic control by testing the blood glucose level at home. Furthermore, Tourkmani (2014) reported that there is a need to promote health education by publishing flyers and brochures about the risk factors of T2DM, thus improving general knowledge about diabetes type 2.

Food environments could make a positive contribution to a healthy lifestyle (eating healthy) for type 2 diabetes patients. Larson *et al,* (2009) claim that people who had many choices of supermarket and fewer fast food restaurants in their neighbourhood had healthy intake habits and less risk of developing T2DM and obesity. In order to encourage Type 2 diabetic patients in the KSA to improve their diet and lifestyle, they should be encouraged to increase the intake of traditional Saudi foods such as, Harees, Hassawi rice, dates and Margoog, which are a rich source of iron, fibre and whole grains (Al-Mssallem, 2014). The findings of this study suggest that the healthy traditional Saudi foods,

such as rice and whole grains (Al-kanhal *et al.*, 1994 and Alhadd *et al* 2007) should be included in the diet of patients with Type 2 diabetes. Furthermore, being active for at least 30 minutes per day as well as providing a health education could also help to reduce the incidence of T2DM in SA and make an important contribution to the control of Type 2 diabetes, by reducing blood glucose levels. Sidawi *et al,* (2014) reported that by providing facilities such as gym centres, sidewalks and cycling lanes, the lifestyle habits of the Saudi population could be improved.

There are numerous different sources of polyphenolic compounds, with fruits such as dates and plants such as *Nigella sativa* seeds being rich sources (Saleh *et al.*, 2011; Rajab *et al.*, 2013). Qadori, 2011 have shown that *Nigella sativa* has a beneficial effect on diabetes because it contains antioxidants (such as Thymoquinone) and has a hypoglycaemic effect and can reduce the risk of Type 2 diabetes.

Ajwa date is a soft dry fruit that grows on palm trees in Saudi Arabia (Al-Madina Al-Menawrah). Ajwa dates contain essential vitamins such as vitamin A, fibres and minerals such as phosphorus, iron, magnesium, and calcium. However, currently there is insufficient scientific evidence on the relevance of Ajwa dates as a beneficial dietary factor, with only few studies that show that it is a rich source of natural antioxidants (such as *Phoenix dactylifera*) (Saleh *et al.*, 2011; Rahmani *et al.*, 2014 and Rajab *et al.*, 2013). Accordingly, in order to identify the significant effects of the Ajwa date, there needs to be further studies carried out on humans. An important point to beware of in designing such studies is it is normal to eat the flesh of the date not the stone but some workers have used ground stone or stone extract in their studies which complicates the problem. Studies should be separated into those which used date flesh and those which used ground stone or stone extract simply because of the biochemical differences between stones and flesh. There is now a drink based on ground date stones available in the SA which might be a useful source of the active ingredients present in the stone and of value to diabetic patients although the effects of preparation of the drink on the “active” ingredients has not been studied.

Ajwa dates have been used for many years, and many people have tried to grow them in different countries and different soils. However, the chemical composition for Ajwa dates is completely different to the original Ajwa dates that come from Al-madinah Al-menawrah due to the soil, geographic and other environmental factors. Ajwa dates are a rich source of fibre (soluble and insoluble) and, as mentioned in chapter 3, they were originally grown in Al-madinah Al-menawrah but can now be grown around many Saudi cities. Only 5% of the Ajwa dates on the market are grown in Al-madinah, 95% of AJ dates are grown in Haeel city, Qassium city, Makkah and Jeddah. Those grown in Al-Madinah have a different chemical composition and smaller size compared to those from Haeel and Qassium. The variation in AJ dates depends on genetic variability among the cultivars (Ibrahim, 2013; Khalid *et al*., 2016). The date palm research centre of excellence in Saudi has the information for all types of dates around Saudi and the researcher can use it for their research. However, the consumers cannot tell by eye, which AJ is grown in al-Madinah. The AJ dates grown in al-Madinah can only be distinguished by the information provided on the food labels regarding where they are sourced. Thus, food labeling on AJ dates are an important to help reduce the adulteration of the dates available on the market.

Nigella sativa is an herbaceous plant, the seeds of which have been widely and traditionally used in the Middle East, North Africa and India for the treatment of several illnesses such as asthma, coughs and fevers. Alherz *et al* ,(2012) concluded that *Nigella sativa* seeds have numerous nutritional benefits as they contain proteins, fats and carbohydrates. In addition, they are rich in potassium, phosphorus, sodium and iron but low in calcium and zinc (ibid, 2012). In this study the inclusion of *Nigella sativa* seeds in the diet appears to be beneficial and is therefore recommended.

Nigella sativa seeds are grown around the world (Mediterranean countries, North Africa and Asia) and each have a different chemical composition, bioactive components, and biological activities due to environmental factors such as the soils and the plants' genetic makeup. The variation in *Nigella sativa* within species is inherent by chemical traces (Dubey *et al*., 2016; Ahamad Bustamam *et al*., 2017).

Ajwa and Ns are both natural bioactive products, which contain a rich source of nutrients such as fibre, natural antioxidants, vitamins and minerals. Therefore, since the researcher did not extract a specific component from either of the two dietary supplements, all the possible mechanisms that could be responsible for the reduction in BGL should be discussed.

One of the reasons why there may have been a reduction in the BGL could be due to the presence of soluble dietary fibre (SDF) and insoluble dietary fibre (IDF) in both Ajwa and Ns (as mentioned in chapter 2). Such fibres play an important role in reducing the absorption of glucose, which may have helped to control the BGL as Chandalia et al (2000) found that a high intake of fibre showed a positive impact on glycaemic control.

Furthermore, soluble dietary fibre could be a possible reason for lowering the blood glucose and cholesterol levels in the body. The possible mechanism for lowering the blood glucose level is that after eating a meal that has a good source of soluble dietary fibre (SDF), the fibre β-glucan increases the viscosity of the small intestine in the gastrointestinal tract (GI), which could delay carbohydrate digestion. In turn, this helps to reduce blood glucose levels as the β-glucan slows down the glucose absorption (Lattimer and Haub, 2010). Moreover, the intestinal viscosity could reduce bile acid absorption and then increasing the bile secretion causing a reduction in LDL cholesterol levels. This effect occurs due to the soluble fibre interacting with bile acids.

It has been conclusively shown that a daily intake of 5g β-glucan (soluble fibre) has a positive decline of 2 hour postprandial glucose, insulin and LDL cholesterol levels (Lattimer and Haub, 2010). The IDF helps people who are suffering from constipation due to the bulking effect of passing food quickly into the stomach and intestine (Threapleton *et al*, 2013). Furthermore, IDF helps people to control their weight (Burton-Freeman *et al*., 2017) while soluble fibre has a greater effect on BGL than insoluble fibre.

In addition, the presence of potassium in Ajwa dates could also be used to explain the results on blood pressure, as it has been found to have a positive impact on pressure in the arteries and blood vessels. NHS (2017) suggests that the daily average intake of potassium for an adult should be 3,500mg and that consuming certain foods that are rich in potassium (such as bananas, dried apricots, raisins, potatoes and Ajwa dates) could regulate blood pressure by improving kidney function. (Geleijnse *et al,* 2003).

It is very important to control the blood glucose level and blood pressure because that helps to prevent kidney malfunction. Including potassium in the diet could be very helpful for diabetic patients to manage and keep the potassium levels normal and could prevent the development of low potassium levels (hypokalemia) and high potassium level (hyperkalemia), which could cause a heart attack (National Kidney Foundation, 2017). Regulating insulin for type 2 diabetes could also help to regulate potassium levels for diabetic patients. Reducing the insulin levels in diabetic patients could lead to increased potassium levels in the cells and in the blood (Nguyen *et al*., 2011). Diabetic nephropathy (DN) is a disease that is common in diabetic patients, who had a kidney malfunction and that is one of the diabetes complications. To reduce the risk of DN, potassium levels should be within a normal range (3.5-5.0 milliEquivalents per liter (mEq/L).(Lim, 2014).

One potential mechanism by which polyphenolic compounds could have beneficial effects on insulin sensitivity is by increasing nitric oxide (NO) production in the endothelium of the vascular system, which can increase tissue and organ blood flow and improve glucose uptake and metabolism (Quiñones, 2003). Thus, increasing NO bioavailability may be associated with beneficial effects on insulin sensitivity and carbohydrate metabolism.

The present results provide helpful guidance as to which are the most beneficial dietary factors that Type 2 diabetes patients can use to control their blood glucose.

Chapter 6 Conclusion

6.1. Limitations of the Study

6.2. Suggestions for Future Studies

6.3. Conclusion

6.4. Public Health Recommendations

6.1. Limitation of the Study

The trials (diabetic and healthy groups) were conducted in different countries, hence the measurements were taken in different places, which could have caused a difference in results for trial 1 (diabetic) and trial 2 (healthy) subjects. It would have been better to have had the same clinic carry out all the measurements. In addition, the social, economic and cultural differences of the participants (from UK and SA) may also have had an effect on the results. For example, it was found that the healthy subjects were more active than the diabetic subjects. This could have been due to the fact that the healthy participants were all from the UK. The weather in the UK is different from that of SA, and as a result, the level of PA may have differed, as the lifestyle in the UK is generally much healthier. Furthermore, food portion sizes are larger in SA when compared to the UK, and eating habits differ, such as whole families eating from a single large plate in SA, making it difficult to measure a single portion of food. Therefore, compliance with the modified diet could have been better assessed, possibly through the use of a dietary sheet to make sure that all participants followed the same diet.

Another limitation of this study was that the lifestyle questionnaire alone was not enough to measure the PA. Arm and waist circumference may have been a better method to observe this factor.

Studies (Arredondo et al, 2012 and Sylvia et al, 2014) have found that devices such as armbands, heart-rate monitors, pedometers and accelerometers are among the many alternative ways to measure physical activity. In addition, there are other methods to measure the PA like self-report questionnaires, self-report activity diaries and direct observation. Some of these methods are difficult to get ethical approval, for example direct observation. However, after a pilot study of 15 participants who live in the UK, found that some of them found it difficult to write the activity type and time, and that they did not fill in the self-report activity diaries, the researcher decided to use a questionnaire. Therefore, a limitation of this study was that the assessment of the PA was not critical and accurate. For Saudi's participants it was not useful for them to write the activity diaries.

In the future, the PA should be measured by armband devices to be more accurate. The variation between the two cultures (KSA and UK) would also be a problem when using the self-report diaries to measure PA, because the two cultures are different and the 2 trials cannot be compared,as the devices for measuring PA would be different. For the validity and reliability should be all the analysis in the same lab.

In the future, it would be better if the same clinic carries out all the clinical biomarkers and testing of all the participants. This could be a standardised methodology for both participants to make sure all the measurements have been addressed in the same clinic lab.

This study could have been improved in a number of ways. Firstly, trial 2 participants (healthy individuals) should have had their blood pressure measurements (DBP and SBP) and HbA1c levels taken in the same hospital (in the same way as the diabetic participants). This would have provided more information by which the two trials could have been compared. Secondly, in order to get a more accurate result, the trial 1 intervention groups (Type 2 diabetic patients) should have all had a poorly controlled HbA1c level, for example 7+ %, rather than using any random Type 2 diabetes patients. Thirdly, there were more female participants than male participants in trial 1 and trial 2, thus resulting in a non-representative sample, which may have implications for the general conclusions of the study, as they may not apply to a group of only male participants. Fourthly, this study only addressed the blood glucose level, HbA1c and blood pressure of diabetic participants only. Finally, the participants from each of the trials were from two different countries (SA and UK). Therefore the measurements were not carried out for participants from both trials in the same place. It would have been better for the researcher to have recruited healthy participants who attended the same nutrition clinic as the diabetic participants, in order to be able to follow the measurement records from all participants.

One of the possible limitations of this study is that there was no way for the researcher to measure patient's compliance with the modified diet since patients did not provide feedback on their compliance with their prescribed diets. Therefore, future researchers of similar studies, may want to consider

methods to check compliance by using a biomarker of compliance such as blood or urine samples.

6.2. Suggestions for Future Studies

This study is the first of its kind to have reported on the effect of Ajwa on the BGL of Type 2 diabetes patients. There is a lack of scientific research on the benefits of the Ajwa dates on humans, thus further research is required. Furthermore, future studies in this field could also focus on establishing whether or not there are any observable benefits of Ajwa date seeds, since most studies on humans, including this one, only focus on the Ajwa date. Due to the lack of observable effects of the Ajwa date on BGL from this current study over the 12 weeks, future research could investigate the impact of Ajwa date seeds on BGL in Type 2 diabetes patients.

Another factor that future research in this field could consider, is to use *Nigella sativa* in different forms, such as in capsules or in the form of powder as well as the raw seeds, and measure its impact on BGL in Type 2 diabetes patients. A comparison between these different forms of *Nigella sativa* may help to broaden the understanding of which form of *Nigella sativa* is most effective.

Moreover, several questions remain to be resolved with regards to the dose of *Nigella sativa* seeds that have the most observable effect on BGL of Type 2 diabetes patients. A further suggestion for future research would be to investigate the effect of different doses of *Nigella sativa* such as 1.5g/day, 2g/day and 2.5g/day on lipid and glucose profile in Type 2 diabetes patients.The reason for these suggested amounts is due to the fact that Bamosa et al (2012), studied the effects of 1g, 2g and 3g/day of *Nigella sativa* seeds, and found that 1g/day had no significant effect on BGL, 2g/day had a significant effect and 3g/day had no observable effect on BGL. Therefore, it may be beneficial to reduce the gap between the different doses from 1g (as in Bamosa et al's (2012) study) to 500 mg in order to be able to see which dose of *Nigella sativa* seeds has the most observable effect on BGL

A suggested study design for this may include a randomised clinical trial of 90 participants with Type 2 diabetes and a HbA1c level of >7% (45 male and 45 female). These 90 participants should be placed on a modified diet and divided into 3 equal groups (30 participants in each group -15 male and 15 female)

namely A, B and C. Each group should then be given one of the 3 doses of *Nigella sativa* seeds in the form of capsules (1.5g, 2g and 2.5 g) daily for 120 days. BGL measurements should then be recorded weekly for each of the groups and HbA1c levels should be recorded at the start and end of the study.

Finally, future research could also compare the impact of Ajwa date seeds with *Nigella sativa* seeds, in order to see whether there are any significant effects in the BGL of Type 2 diabetes patients. This is because there are currently no studies that have compared these two seeds.

6.3. Conclusion

This current study aimed to determine the effect of dietary factors on blood glucose levels in healthy people and Type 2 diabetic patients by giving them a dietary supplement of either 1 Ajwa date per day or 2g/day of *Nigella sativa* seeds. In summary, Type 2 diabetes can be effectively controlled by taking medicine, applying dietary modifications and completing regular physical activity. As discussed previously, patients with Type 2 diabetes should follow a healthy diet and be active at home and outdoors as these lifestyle changes are important to consider to avoid the complications of the disease. In addition, there are many factors that can also contribute to the control of blood glucose levels, such as the awareness of Glycaemic Index (GI). Foods with a low GI are broken down at a slower rate by the body, so they are less likely to induce a sudden increase in blood sugar concentration, and are thus the most ideal foods to consume for those aiming to maintain stable blood glucose levels. Furthermore, eating a diet that is rich in fibre and has a low GI can reduce the risk of cardiovascular disease and diabetes. The combination of these factors can play a significant role in managing the condition and have an immensely beneficial impact on the lives of those suffering from Type 2 diabetes.

The most obvious finding to emerge from this study is that consuming 2g/day of *Nigella sativa* seeds for 12 weeks, appear to be the most effective dietary supplement in order to help lower BGL levels (Fasting blood glucose (FBG), after 2 hours postprandial 2HPP and HbA1c) and blood pressure. Therefore, there is benefit in using traditional plant treatments from natural resources to aid in the management of the disease. Furthermore, daily supplementation of 2g/day of *Nigella sativa* seeds for 12 weeks also lowered weight and BMI in both the control and intervention groups. The results from this project will provide helpful guidance as to what the most beneficial dietary factors are for controlling blood glucose levels in Type 2 diabetes patients.

6.4. Public Health Recommendation

- Throughout the study, it was difficult to persuade the diabetic participants to be active outdoors due to the hot weather in SA. This suggests that there is a need to improve the education programme for diabetic patients in order to increase the awareness of the importance of physical activity.
- All the diabetic patients should register at a local diabetes clinic and be educated in diabetes programmes.
- Encourage the use of the treatments with traditional plants and herbs such as *Nigella sativa* seeds, which have a beneficial effect on the blood glucose levels of patients with Type 2 diabetes.
- All Type 2 diabetes patients should be given a list of traditional Saudi foods with their GI in order to help them to be able to easily identify healthy foods with a low GI so that they can control their BGL.
- Increase the dietary intake of fibre, whole grains, and foods with low Glycaemic Indices (GI).
- Encourage the recording of blood glucose levels using Self Monitoring Blood Glucose (SMBG) meters on a daily basis in order to impact dietary intake to help control the blood glucose level and improve the HbA1c.
- Following a diet plan and changing lifestyle will be helpful for controlling the disease and prevent the complications that are related to Type 2 diabetes.
- Enhancing the awareness of risk factors and SMBG by increasing the health education programs in SA for diabetic patients.

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Appendix

Appendix 1

Research Participants Information Sheet

Study title: The control of type 2 diabetes with specific references to dietary factors

Invitation Paragraph

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of this study?

The primary aim of the current study is to investigate the regulatory effects of consumption of Ajwa date and *Nigella sativa* seeds on glucose levels in type 2 diabetic patients. The secondary objective is to investigate whether these dietary factors may have potential beneficial effects in controlling diabetes complications and improving insulin sensitivity.

What is the foods , device or procedure that is being tested?

In this research I will test the first group in the UK and I divided into two groups: first group they have to be healthy and they will receive Ajwa dates, *Nigella sativa* and the second group (diabetic patients) will receive the same modified diet and dietary food.

Why have I been invited to take part?

You have been invited to join our study because I will investigate the benefit of Ajwa dates and other dietary intake such as *Nigella* seeds. Furthermore, many people will involve in this study to help diabetes patients.

Do I have to take part?

Your participation is voluntary. I would like you to consent to participate in this study as we believe that you can make an important contribution to the research. If you do not wish to participate you do not have to do anything in response to this request. We are asking you to take part in the research because the benefits from this study will help the diabetic to control the blood glucose level and we believe you can provide important participation to us that may be relevant to the evaluation of this study.

You will be given a copy of this information sheet and your signed form to keep. You are free to stop taking part at any time during the research without giving a reason. If you decide to stop, this will not affect the care you receive.

What will happen to me if I take part?

If you are happy to participate in the research we will ask you to read this information sheet, sign the consent form and return it to us. When we receive this a member of the evaluation team will contact you to discuss your participation in the evaluation. At that point we can confirm your participation and make arrangements for you to meet the researchers.

That the first group will take Ajwa dates, cherry, nigella seeds for three months every day with modified diets and they can choose the amount of Ajwa dates 1 , I will bring that dates because it will bring Ajwa dates from Saudi Arabia. In addition, every week I will meet you and the blood test should take every week after 2 hours of eating dietary intake. According to blood glucose level test, the participants will test it by finger-picking devices and lancets, it gives us an accurate result of your blood glucose level.

Figure 1: Ajwa Dates

The second group (diabetic patients) will take, Ajwa dates and *Nigella* seeds every day for 12 week. In addition, home blood glucose test will do it twice a week.

What are the possible disadvantages and risk of taking part?

There is no risk of eating fruits.

What are the possible benefits of taking part?

The information you provide can contribute to the future development of the treatment for diabetes type 2 and the result can help us to know which one of the following dietary intake is better for diabetes type 2 .

However**,** we cannot promise the study will help you but the information we get from this study will help and improve the treatment of people with diabetes type 2.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed.

Will my taking part in the study be kept confidential?

All information you provide to us will be kept confidential and we will follow ethical and legal practice. Only members of the research team will have access to it.

What will happen to the results of the research study?

All information provided by you will be stored anonymously on a computer with analysis of the information obtained undertaken by the researcher based at Manchester Metropolitan University.

Who is organising and funding the research?

The sponsors of this study will pay Saudi Embassy (Ministry of High Education in Saudi) for including you in this study.

Further information and contact details:

Researcher: Reham Algheshairy

Email: 10981715@stu.mmu.ac.uk

Direct supervisor: Christopher Smith

Appendix 2

CONSENT FORM

Title of Project: **The control of type 2 diabetes with specific references to dietary factors**

Name of researcher**: Reham Algheshairy**

Please initial box

1. I confirm that I have read and understand the information sheet dated…….. for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. I acknowledge the risks associated with the study and they have been explained to me. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I agree to take part in the study. ☐

_____	_____	_____
Name of participant	Date	Signature

_____	_____	_____
Name of person taking consent	Date	Signature

When completed, 1 for participant; 1 for researcher site file; 1 (original) to be kept in medical notes

Appendix 3

Investigation of the control of type 2 diabetes with specific references to dietary factors

Hello everybody,

My name is Reham Algheshairy and I am studying a PhD in Nutrition and Food Science at Manchester Metropolitan University, I am undertaking a piece of research work which is requires studying this diet and dietary factors on diabetic patients.

This diet is designed to provide sufficient vitamins and minerals for good health .In addition, this diet has been designed to gather information to control blood glucose level on Saudi people with type 2 diabetes and those who are healthy people in the UK.

All information provided during this study will be kept strictly confidential, and no information will be used for any other purposes other than those intended.

Reham Algheshairy

07453306855

reham_goshiry@hotmail.com

10981715@mmu.ac.uk

Name:_____ Date of Birth:_____ Current weight:_____ height:_____

Address:_____

_____

Contact number:_____

Section A: personal background information

1. **Are you: (please tick one box)**

   ☐Male ☐ Female

2. **Age:**

   ☐18 – 30 ☐31 – 40 ☐41 – 50 ☐ Over 50

3. **Are you smoking**

   ☐Yes ☐ No

4. **Educational Status:**
   ☐Undergraduate ☐Post- graduate degree (i.e. Master and PHD
5. **What is your marital status?**
   ☐Single
   ☐Married
   ☐Married with children
   ☐Divorced
   ☐Widowed
   ☐Other: specify ----------

Section B: Lifestyle

1. **Do you smoke?**
   ☐ Yes ☐ No

2. **Do you do Physical exercise?**
   ☐ Yes ☐ No

3. **How often do you do physical exercise?**
   ☐Never
   ☐Only during the holidays
   ☐2 to 3 times a month
   ☐Once a week
   ☐ 2 or 3 times a week
   ☐ 4 to 6 times a week
   ☐ Daily

Section C: Diabetes people

1. **Do you have a machine to measure your blood glucose level?**
   ☐ Yes ☐ No

2. **Do you test your blood glucose level?**
   ☐ Daily
   ☐ Once a week
   ☐ 2 to 3 times a week
   ☐ 4 to 6 times a week
   ☐ Monthly

3. **Do you take a pills for diabetes?**
   ☐ Yes ☐ No ☐ Don't know
4. **Do you get insulin injections?**
   ☐ Yes ☐ No ☐ Don't know
5. **Do you take pills for high blood pressure?**
   ☐ Yes ☐ No ☐ Don't know
6. **Do you take pills for cholesterol?**
   ☐ Yes ☐ No ☐ Don't know

7. **Age of diabetes onset?**
   _____

Appendix 4

1600-1800 Calorie Diet Plan

(A)Menu for breakfast: choose one option from group A

- 2 sliced brown toast 144 + cream cheese 2tbsp + 1cup of low fat milk **330cals**
- 1 slice of brown bread 144 + 55g or ¼ cup cottage cheese 50 + 1 cup of orange juice **360cals**
- 2 tbsp of hummus + 2slice of brown bread + 1 cup of low fat milk **355cals**
- 1 boiled egg + 2slice brown toast +1 tomato + 1cup of low fat milk **350cals**
- 1cup semi-skimmed milk + ¾ cup of bran flakes cereal + 1 apple **200cals**
- 1 cup of salad + 2 slice of turkey smoked + 2 slice of brown bread + 1cup semi-skimmed milk 100 = **342cals**
- 1 Small chapatti + 30 g of low fat cream cheese + 1 apple **326 cals**

(B) Menu for lunch: choose one option from group B

- 1 cup of green salad + 1 cup of brown rice + grilled breast chicken 60 gram **415cals**
- A cereal bowl of salad with dressing + 1cup of pasta with tomato sauce with beef **468cals**
- 1 cup of green salad with Italian dressing + grilled fish 60g + 1cup of rice **485cals**
- 2 slice of brown bread + 1 cup of cooked beans with beef and tomato + 1cup of green salad **609cals**
- 60 g of grilled steak + 1 cup of caesar salad low fat dressing+ 1 slice of brown toast **500cals**
- 1 cup of salad + 1cup of okra with beef and tomato sauce +2 slice brown bread **572cals**
- 1 cup of salad +1cup of jew's mallow cooked with chicken +1cup of rice **445cals**

(C) Menu of Snack: choose one option from group C

One portion of fruit (apple or banana or handful of grapes or a slice of melon or small glass of fruit juice

- One apple medium **116cals**
- Grapes 1/2cup **55cals**
- Banana **105cals**
- Pineapple 1 cup **113cals**
- Fruit salad (pineapple, banana, oranges, kiwi, melon, grapes) 1cup **125cals**
- Oranges **62cals**
- One Kiwi **46cals**
- Blueberries ¼ cup **21cals**

(D) Menu for diner: choose one option from group D

- 1cup of Lentils soups +2 sliced brown toast + 80 g green salad **310cals**
- 6 ozSalmon grilled with lemon and olive oil + 2 slice of wholegrain bread **437cals**
- 1 cup of vegetable soups + 2 slice of wholegrain bread **332cals**
- 2 cup of broccoli soup with low fat cream With + 2-3 crisp breads **330cals**
- Tuna sandwich with salad + 1cup of vegetables soup + 10 g lemon **440cals**
- 2cup of celery soup + 2-3 crisp breads + 1cup of corn **338cals**
- chicken sandwich with salad + 1 cup vegetables soup + 10g lemon juice **347cals**

(E) Menu for snack: choose one option from group E

1. 4 Ginger biscuits + 1 glass of low fat milk **348cals**
2. 4 Oat biscuits + 1 glass of low fat milk **360 cals**
3. 4 Oat crackers + 1 glass of low fat milk **340 cals**
4. 3 wheat biscuits + 1 glass of low fat milk **295 cals**
5. 28 g of unsalted mix of nuts (almond, cashews, pecans, walnuts and peanuts) + 1 glass of low fat milk **268 cals**
6. Slice one Apple + 1 tablespoon 16g of natural peanut butter **304 cals**
7. 25 unsalted pistachios+ 1 glass of low fat milk **263 cals**

Free food list (you can eat I whenever you like)

- **Sugar-free Gelatin**
- **Coffee without sugar**
- **Tea without sugar**
- **Arabic coffee**
- **Water**
- **Lemon juice**
- **Herbs, fresh or dried**
- **Garlic**
- **Vinegar**

Additional 600 Calorie for male only

- Celery 60 gram with 1 tablespoon peanut butter
- Sweet potato baked 2 small portion
- 1 slice of brown bread + 2 tablespoon hummus
- 1 slice of brown bread + 2 tablespoon baked beans with tomato sauce
- 1 bowl Red kidney beans with lemon and sweet corn salad
- 1 bowl rice noodles cooked with vegetables stir fry
- 1 bowl mix salad with potato + 1 tablespoon dressing low fat

Appendix 5

Nutrition information:

- This diet is rich in fiber, vitamins, minerals and low fat
- You should eat a healthy diet high in fibre, fruit and vegetables and low in fat , salt and sugar.
- It is very important to exercise regularly because physical activity decreases your blood glucose level.
- Eating regular meals and including starchy carbohydrate at each meal
- You should not skipping meals because that can help regulate your blood sugar levels
- Starchy foods (Bread, chapatti, rice, pasta, breakfast cereals, potatoes, sweet potatoes and yam) at each meal will help stabilise blood sugar control
- Limiting how much sugar and sugary foods are eaten
- Reducing fat in the diet, especially saturated fats, due to increased risk of heart disease
- Avoiding adding salt when cooking or at the table
- Never drink on an empty stomach. You should always have something to eat before drinking
- Do not count the carbohydrate in alcoholic drinks
- Always have something starchy to eat whilst drinking alcohol or shortly afterwards e.g. crisps / sandwich. Occasionally, if you have drank over the recommended amounts a late night meal on the way home may be useful i.e. burger, chips, curry and rice.
- Always have a starchy snack before going to bed even if your blood sugars appear normal

The Glycaemic Index (GI) is a scale that relates to the speed at which carbohydrate foods are absorbed. Low GI foods are absorbed into the blood stream slowly and high GI foods are absorbed quickly. Being aware of healthy low GI foods can help improve diabetes control. Choosing lower GI foods means your blood sugar levels will raise more slowly, avoiding high blood sugar readings.

Starchy foods (carbohydrates)

Bread and chapatti, other cereals, (such as rice, pasta and breakfast cereals) and

Potatoes

• Try to use granary bread, basmati rice, pasta and high fibre breakfast cereals

• Have foods from this group at each meal

• Eat regular meals based on similar amounts of starchy foods each day

• This will help to control your blood glucose level

Appendix 6

List Below Any Changes For the participants:

Week	Changes in diet	Changes in weight	Changes in blood pressure	Change in Appetite
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				

Have you finished your meal? Yes or No

Have you skipped any meals? Yes or No

Appendix 7

Recording the Blood glucose level

Week	Dates	Blood glucose level (fasting)	Blood glucose level after 2 hours of eating breakfast
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			

Appendix 8

Instruction for the participants

Group 1(Modified diet)

- You should choose one meal from each menu
- You should avoid eat any sweets or soft drink
- You can drink green tea or black tea without sugar or you can use alternative sugar.
- You should avoid eat Ajwa dates

Group 2(Ajwa dates+ Modified diet)

- You should choose one meal from each menu
- You should avoid eat any sweets or soft drink
- You can drink green tea or black tea without sugar or you can use alternative sugar.
- Avoid eat *Nigella*.
- You should eat 1 Ajwa date between 7:00am and 12:00pm and you should eat it as a snack not with meal.

Group 3(Nigella Sativa+ Modified diet)

- You should choose one meal from each menu
- You should not eat any sweets or soft drink
- You can drink green tea or black tea without sugar or you can use alternative sugar.
- You should avoid eat Ajwa dates.
- You should eat 2g of Nigella with cup of milk low fat between 7:00am and 12:00pm and you should eat it as a snack not with meals.

Appendix 9

Help a sister out by eating *Nigella* Seeds

I am a PhD student at Manchester Metropolitan University and I am doing research on the effect of nigella seeds and measuring the Blood Glucose level by self-monitoring weekly during three months.

- The researcher will provide **2g *Nigella* seeds** for each volunteer along 12 weeks.
- Eating 2 g, ***Nigella* seeds** daily during three months.
- Provide a modified diet (easy to follow)
- Regular observation from the researcher
- The researcher will provide self-monitoring for measuring blood glucose
- Need 30 volunteers.

If you need more information

Contact me please

Reham Algheshairy

Mobile and what's app number: **07453306855**

REHAM.M.ALGHESHAIRY@stu.mmu.ac.uk

Appendix 10

Help a sister out by eating Ajwa dates

I am a PhD student at Manchester Metropolitan University and I am doing research on the effect of Ajwa dates and measuring the Blood Glucose level by self-monitoring weekly during three months.

- The researcher will **provide Ajwa dates box** from Al-Madina Al-Monawara for each volunteers.
- Eating 1 **Ajwa date** daily during 12 weeks.
- Provide a modified diet (easy to follow)
- Regular observation from the researcher
- The researcher will provide self-monitoring for measuring blood glucose
- Need 30 volunteers.

If you need more information

Contact me please

Reham Algheshairy

Mobile and what's app number : **07453306855**

REHAM.M.ALGHESHAIRY@stu.mmu.ac.uk

Appendix 11

المملكة العربية السعودية
المديرية العامة للشئون الصحية بمنطقة مكة المكرمة
مديرية الشئون الصحية بالعاصمة المقدسة
مستشفى النور التخصصي

وزارة الصحة
Ministry of Health

الرقم : .....
التاريخ : .....
المرفقات : .....

Dear Sir / Madam

I confirm that **Miss . Reham Algheshairy** has the permission to conduct her data collection in the **Diabetes Center** at **Alnoor Specialist Hospital , Makkah** as part of her PHD studies from **4 July to 4 October 2015**

Best regards ,

Dr . Khaled Abdullah Tayeb

Consultant of Endocrine and Dialectology

Head of the Diabetes Center

Al noor Specialist Hospital

Tel : 00966590003534

Email address : Khaledtayeb2@hotmail.com

DR. KHALID ABDULLAH TAYEB
Consultant Diabetologies, Endocrinology

Appendix 12

الاسم: ..... تاريخ الميلاد : ..... الوزن الحالي : .....

الطول : ..... العنوان : ..... رقم الهاتف او جوال : .....

القسم الأول : معلومات شخصية

1/ هل انت :

○ ذكر ○ أنثى

2/ العمر :

○ 18-30 ○31-40 ○ 41-50 ○فوق ال50

3/ المستوى التعليمي :

○ المتوسطة ○ الثانوية ○ بكالوريوس ○ دراسات عليا ○ أخرى

4/ الحالة الاجتماعية :

○ أعزب ○ متزوج ○ متزوج ولديه أولاد ○ مطلقه ○ أرمله ○ أخرى

القسم الثاني نمط الحياة:

1/ هل انت مدخن :

○ نعم ○ لا

2/ هل تمارس الرياضة :

○ نعم ○ لا

3/ كم مرة تمارس الرياضة :

○ إطلاقا لا امارس الرياضة

○ فقط في العطلات

○ مرتين إلى ثلاث مرات في الشهر

○ مرة في الاسبوع

○ مرتين إلى ثلاث مرات في الاسبوع

○ يوميا

القسم الثالث : لمرضى السكري

1/ هل لديك جهاز لقياس السكر في المنزل :

○ نعم ○ لا

2/ كم مرة تقوم بقياس مستوى السكر في الدم :

○ يوميا

○ مرة في الاسبوع

○ مرتين الى ثلاث مرات في الاسبوع

○ كل شهر

3/ هل تاخذ حبوب للعلاج من مرض السكري :

○ نعم ○ لا ○ أحيانا

4/ هل تأخذ حقن الانسولين للعلاج من مرض السكري :

○ نعم ○ لا ○ أحيانا

5/ هل تعاني من ارتفاع او هبوط في ضغط الدم :

○ نعم ○ لا

6/ هل تأخذ حبوب للعلاج من ضغط الدم :

○ نعم ○ لا ○ أحيانا

7/ هل تأخذ حبوب للكوليسترول :

○ نعم ○ لا ○ أحيانا

8/ متى أصبت بداء السكري ؟ في عمر .....

Appendix 13

استمارة موافقة للإشتراك في البحث العلمي

عنوان البحث:
التحكم في مستوي الجلوكوز في الدم عن طريق تأثيرالحبة السودا وتمرة العجوة علي مرض السكر من النوع الثاني

مكان إجراء البحث:
مستشفي النور بمكه المكرمه

اسم الباحث : ريهام محمد صالح الغشيري

لقد قرأت استمارة القبول هذه وفهمت مضمونها. تمت الأجابة على أسئلتي جميعها. وبناء عليه فأنني، حرا مختارا، أجيز إجراء هذا البحث و أوافق على الإشراك فيه،
وإني أعلم إن الباحث وزملاءه ومعاونيه أو مساعديه سيكونون مستعدين للإجابة على أسئلتي،
وأنه باستطاعتي الاتصال بهم على الهاتف _____ .
كما أعرف تمام المعرفة بأنني حر في الانسحاب من هذا البحث متى شئت حتى بعد التوقيع على الموافقة دون ان يؤثر ذلك على العناية الطبية المقدمة لي. أعلم أني سوف أحصل على نسخة طبق الأصل عن هذه الموافقة.

Appendix 14

حمية ذات 1600 _ -1800سعرة حرارية

يمكنك إختيار وجبة واحدة من الوجبات التالية:
(أ) وجبة الإفطار (7 صباحًا الى 12 مساءً)

• شريحتين توست أسمر + 1 ملعقة صغيرة جبنة قليلة الدسم + كوب حليب قليل الدسم
•2 شريحة من التوست أو الخبز الأسمر +1 كوب من عصير البرتقال الطازج + شريحة جبنة قليل الدسم
• 2 شريحة توست أسمر أو ربع رغيف أسمر + 2 ملعقة كبيرة من الحمص أو فول +1 كوب من الحليب قليل الدسم
• 1 بيضة مسلوقة + طماطم طازجة +1 شريحة توست أسمر + 1 كوب من الحليب قليل الدسم
• 1 كوب حليب خالي الدسم + ¾ كوب من حبوب الشوفان أو كورن فليكس + 1 تفاحة
• 1 كوب من السلطة من اختيارك (خيار طماطم - خس) + شريحتين من التركي المدخن + شريحة من التوست الأسمر +1 كوب حليب خالي الدسم
• 1 فطيرة +ملعقة من الجبن الكريمي قليل الدسم + 1 تفاحة + كوب من حليب خالي الدسم

(ب) وجبة الغداء (يمكنك اختيار وجبة واحدة فقط)

• 1 كوب من السلطة الخضراء + 1 كوب من الرز الأسمر + شريحة من صدر دجاج مشوي
•1 كوب من السلطة (جرجير + خس + طماطم) صوص خل بلسمك وزيت زيتون + كوب من الباستا (معكرونة مع اللحم المفروم والصلصة)
• كوب سلطة من اختيارك + 70 جرام سمك مشوي +1 كوب رز صيادية أو رز أبيض
• 1 كوب من ايدام أو مرقة الفاصوليا مع اللحم +1كوب من السلطة الخضراء من اختيارك (خيار + خس + جزر + طماطم) + ربع رغيف أحمر
• 70جرام شريحة ستيك لحم مشوي + 1 كوب من سلطة من اختيارك + 2 شريحة من التوست الأسمر أو الرغيف الأسمر
• 1كوب سلطة من اختيارك (تبولة أو سلطة خضراء أو فتوش) + 1 كوب من مرقة أو ايدام بامية مع اللحم أو الدجاج + ربع رغيف من الخبز الأسمر
• 1 كوب سلطة اختيارك + 1 كوب من الملوخية مع الدجاج + 1 كوب رز

(ج) وجبة السناك : (بين الغداء و العشاء)
(يمكنك اختيار واحد ما يعادل حصه واحدة من الفواكه)
• 1 تفاح
• ½ كوب من العنب
• 1 موز
• 1 برتقاله
• كوب من الأناناس
• سلطة فواكه مشكلة بدون سكر (١ كوب)
• كيوي
• التوت البري (٤/١ كوب)

(د) وجبة العشاء (يمكنك اختيار وجبة واحدة فقط يوميًا)
• 1 كوب من شوربة العدس + ربع رغيف أسمر + جرجير

- 1 كوب شوربة الخضار + ربع رغيف نخاله
- 2 شابورة نخالة + ملعقتين جبنة سايلة قليلة الدسم
- 1 كوب من شوربة البروكلي مع الكريمة قليلة الدسم
- 1 كوب سلطه تونه مع خضروات من اختيارك
- شاورما دجاج على الصاج
- شوربه الخضار + ربع رغيف نخاله

(ز) وجبه خفيفه بعد العشاء (يمكنك اختيار وجبة واحدة فقط يوميًا)

- 4 حبات من بسكوت الزنجبيل + كوب حليب قليل الدسم
- 4 حبات من بسكوت النخالة + كوب حليب قليل الدسم
- 28 جرام من المكسرات الغير مملحة (لوز، كاجو ، فستق)
- 4 حبات من بسكوت القمح

15 Appendix

تعليمات الحمية الغذائية

الحد من تناول الملح:

الإكثار من تناول الملح يسبب احتباس الماء في الجسم، مما يؤدي إلى ارتفاع ضغط الدم الذي يعد من أهم مسببات مرض السكر. لذلك يجب مراعات كمية الملح المضاف أثناء الطهي بالإضافة الى تجنب إضافة الملح المائدة. يتوجب أيضا الابتعاد عن تناول الأطعمة المحفوظة والمعلبة والطعام السريع.

الحرص على تناول الأطعمة الغنية بالألياف الصحية:

تساعد الألياف على معادلة نسبة الجلوكوز (السكر) والدهون في الدم. بالإضافة الى أنها تمنع الإمساك. وهناك العديد من الأطعمة الغنية بالألياف مثل:

1- النخالة والقمح الكامل والشعير الأرز البني الغير مقشور والخبز المصنوع من الحبوب الكاملة، بالإضافة الى البقوليات مثل الفاصوليا المجففة والبازيلاء والعدس.
2- الخضار والفواكه خاصته النية الغير مطبوخة أو المطبوخة بغير مبالغة والابتعاد عن عصرها وتقشيرها.

الاقلال من الأطعمة العالية في الدهون:

إن الاكثار من تناول الدهون يؤدي إلى أمراض القلب والشرايين وهي من أكثر الأمراض التي تنتج عن مرض السكر التي تعتبر خطيره، لذا يجب:

- التخفيف من تناول اللحوم الحمراء خاصة العالية في مستوى الدهون وأستبدلها بلحوم الاسماك والطيور.
- قم بإزالة الدهون من اللحم وجلد الطيور قبل الطهي وتجنب إضافة الدهون عند الطهي مثل السمن أو الزيت والزبد الطبيعي والصناعي /مارجرين.
- أستخدم طرق الطبخ التي لا تحتاج الى إضافة الدهون مثل الشواء أو الخبز في الفرن أو البخار بدلاً من القلي.
- عند تقديم الطعام لا تقوم بإضافة الدهون مثل الزيت أو صلصة/"سوس".
- تجنب تناول الأطعمة الغنية بالدهون مثل المقالي واللحوم الباردة والنقانق والسجق.
- تناول القليل من الآيس كريم والجبن القليل أو المنزوع الدسم كذلك تناول الحليب القليل أو الخالي الدسم بدلاً من الحليب الكامل الدسم.

ممارسة الرياضية:

ممارسة الرياضة بشكل مستمر أو يومي تؤدي الى انخفاض/ معادلة السكر بالدم. كما انها مفيدة لصحة الجسم والقلب والتخلص من الدهون الزائدة في الجسم.

إذا كنت من مرضى السكر يجب الحرص على تناول الكربوهيدرات قبل التمارين الرياضية مثل الخبر او البسكوت او الفاكهة الطازجة أو اللبن.

تعليمات ونصائح عامة

- لتنظيم مستوى السكر بالدم، يجب على مرضى السكر مراعات استهلاك 5 وجبات في اليوم على الأقل، ثلاث منها رئيسية واثنان وجبة خفيفة.
- يجب الاستعانة بقائمة البدائل المرفقة في حال استبدال أي صنف في قائمة طعامك.
- المرضى الذين يتناولون الأنسولين يتوجب عليهم أن يتناولون وجباتهم في أوقات منتظمة يومياً.
- عدم تناولك لإحدى وجباتك اليومية يؤدي إلى تعويضها بكميات أكبر في الوجبة التي تليها مما يضر بحميتك ويؤدى إلى عدم انتظام مستوى السكر بالدم.
- يجب الحرص على تناول الماء بوفرة بين الوجبات.

نصائح لكي تستطيع الالتزام بالحمية الغذائية:

- التخطيط المسبق للوجبات وتحضيرها.
- مضغ الطعام بشكل جيداً وببطء وتناول لقيمات صغيرة.
- استخدام طبقاً صغيراً اكي يساعدك على تقليل كمية الطعام المستهلك.
- عدم تناول الطعام مع مشاهدة التلفاز أو غيره لان ذلك يؤدي الى تناول كميات كبيره من الطعام.
- أقرأ مكونات الأغذية المعلبة في السوبرماركت قبل شرائها فليس كل منتج كتب عليه "للحمية" يناسب مرضى السكر، من الممكن ان يكون منخفض في مستوى الملح أو الدهون أو السكر ولكن لا يعني أنه خال من السكر أو السعرات الحرارية.
- يمكنك تناول الأغذية الخاصة بالحمية والتي تحتوي الحصة الواحدة منها على أقل من 20 سعر حراري بحدود ثلاث حصص يوميا.

Appendix 16

Table 3.1: Time schedule for Diabetic participants (Intervention groups)

	Minutes
Induction and general question	3-4
Sign the Consent form and Applying questionnaire	2-3
Anthropometric measurements (weight and height)	5-8
Reviewing the blood profile and measurements for BP, FBG, 2hPP andHbA1c	2-4
Total	20 -25

Appendix 17

Table 3.3: Time schedule for healthy groups

	Minutes
Induction and general question	3-4
Sign the Consent form and Applying questionnaire	2-3
Anthropometric measurements (weight and height)	5-7
Measuring blood glucose level by monitoring	3-4
Total	15 -20

Appendix 18

Recording for replacing the tubes for *Nigella sativa*

Week	**Dates**	**Replace the *Nigella sativa* tubes.**	**Blood glucose level after 2 hours of eating breakfast**
Week 0 to week 1			
Week 1 to week 4			
Week 5 to week 8			
Week 9 to week 12			